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Exploring the Potential of Stem Cell Therapy in Addressing Neurological Disorders

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ABSTRACT

Neurological disorders are increasingly prevalent and are quite complex, each with different symptoms and a significant impact on quality of life. Given the increasing number of cases worldwide, there's a need to find an effective medical intervention. In light of the aforementioned, this research paper aims to analyse stem cell therapy as a promising medical treatment and further evaluate its applications for various neurological disorders such as Parkinson's Disease, Alzheimer's Disease, Multiple Sclerosis, Stroke, and Spinal cord injuries. In particular, it aims to explore the reparative and regenerative properties of stem cells that make them appropriate for addressing the challenges posed by these conditions. The paper further evaluates some real-life case studies that illustrate successful outcomes. Overall, this paper provides a comprehensive overview of stem cell therapy's impact on expanding the treatment options for neurological disorders.

Keywords: Stem cell therapy, neurological disorders

INTRODUCTION

Stem cell therapy - a promising breakthrough in the field of medicine?

Neurological disorders are diseases impacting the central as well as the peripheral nervous systems. The brain and the spinal cord constitute the central nervous system, and the nerves that branch out from these areas into different parts of the body bring into being the peripheral nervous system (Sherrell, 2021). There are over six hundred neurological disorders that are prevalent, including some degenerative diseases, for example, Parkinson's and Alzheimer's; some diseases caused by defective genes, for example, Huntington's disease and muscular dystrophy; some convulsive disorders, for example, epilepsy; some nervous system development disorders, for instance, the spina bifida; infections, for example, meningitis; and brain tumours, etc. (Garrard, 2012). Many symptoms, including the following, can be brought on by neurological disorders: headaches, light-headedness, weakness or numbness in a limb, memory issues, issues with vision and speech, cognitive challenges, convulsions, tremors, and involuntary movements (Garrard, 2012). Physical examinations, medical histories, and, in some cases, more advanced diagnostic procedures like CT scans or MRIs are used to identify these medical conditions. A quick and appropriate medical intervention is of utmost importance for individuals suffering from a neurological disorder. The treatment method differs based on the particular condition and

severity level. Some conditions can be treated with medication and therapy, while some other disorders might require surgery or other specific interventions (The Economic Times, 2023).

Neurological disorders are steadily becoming a significant and rapidly increasing health concern globally and indeed contribute immensely to the overall disease burden. Ding et al. (2022) examined 18 neurological disorders by understanding the data from the Global Burden of Disease 2019 database with respect to their prevalence, frequency, mortality rates, disability-adjusted life years (DALYs) and other factors such as gender, age, year, location, and socio-demographic Index. In 2019, around 349 million DALYs and 10 million deaths occurred globally because of neurological disorders. From 1990 to 2019, there has been a sign of improvement in the DALY rates and mortality for communicable neurological disorders but the overall burden of neurological disorders is increasing because of the growing population and ageing.

Furthermore, The Lancet Neurology report stated that in 2021 more than 3 billion individuals globally were affected by a neurological disorder. Since 1990, there has been an 18% increase in illness, total disability, and premature death because of neurological disorders, measured as disability-adjusted life years (DALYs). More than 80% of deaths caused by neurological disorders occurred in low-income and middle-income nations, with a significant disparity in treatment accessibility (GBD 2021 Nervous System Disorders Collaborators, 2024).

Treating neurological disorders is crucial because they bring a significant amount of suffering to those affected and their families and deplete human capital from communities and economies (WHO, 2024). Stem cells are a unique kind of cells that possess two important characteristics i.e., self-renewal through which they are able to produce additional cells like them and differentiation through which they are able to change into other cells and perform different functions (Mayo Clinic, 2019). They are required for tissue maintenance, tissue regeneration, and post-injury repair (Mayo Clinic, 2019). Due to their unique properties, stem cells are a favourable treatment option. Stem cell therapy utilises stem cells or their derivatives to stimulate the healing process of damaged, malfunctioning, or wounded tissue (Mayo Clinic, 2019). In light of the aforementioned, this research paper aims to answer the following question: *How can stem cell therapy aid in treating neurological disorders?*

This research paper contends that stem cell therapy can be a promising and prospective medical intervention for neurological disorders like Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Spinal Cord Injuries, and Stroke.

Literature Review on Stem Cell Therapy

Stem cells are undifferentiated cells that can perpetually renew themselves, as well as differentiate into specialised cells with particular functions. Stem cells exhibit plasticity i.e., they can develop into cell types outside of their usual tissue environment (Hegazy, 2015). They help maintain balance and promote healing of tissues (Barzegar et al., 2019).

Stem cells can be classified based on their origin and potency for differentiation.

Stem cells can be classified into three groups depending on their origin:

– **Embryonic stem cells (ESCs)** are pluripotent cells that are derived from the inner cell mass of the pre-implantation blastocyst, normally 5-7 days after fertilisation. They differentiate into endoderm, ectoderm, and mesoderm cells but not trophoblast cells, exhibiting strong clonality, pluripotency, and self-renewal (Mozafari & Yoo, 2020; Ntege et al., 2020;

Vader & Schiffelers, 2016). As a result, they can be used in treatment of tissue regeneration (Ragab et al., 2017).

- **Adult stem cells (ASCs),** also known as somatic stem cells, are undifferentiated cells found in various tissues of almost all kinds of organisms, including humans. They are able to renew themselves and also produce all kinds of cell types found in the organs. They help repair and regenerate tissues following an injury (University of Notre Dame, 2023). Bone marrow contains an abundant amount of adult stem cells (Ragab et al., 2017). The different types of adult stem cells are the Hematopoietic Stem Cells, Neural Stem Cells, Mesenchymal Stem Cells, Skin Stem Cells, Epithelial Stem Cells (University of Nebraska Medical Center, 2018).
- **Induced pluripotent stem cells (iPS cells)** are also pluripotent stem cells derived from adult somatic cells that are re-programmed to resemble the state similar to embryonic stem cells through the activation of specific genes and factors (Ye et al., 2013). They are produced in a laboratory to activate some specific genes and factors found in embryonic stem cells (ESCs) like Oct3/4, Sox2, Klf4, and c-Myc (Ouyang et al., 2019). They are invaluable in the medical field because researching diseases and testing of drugs can be done without any moral objection, as they have pluripotent capabilities and an ability for proliferation (Ouyang et al., 2019).

Stem cells can be classified into five groups depending on differentiation potency:

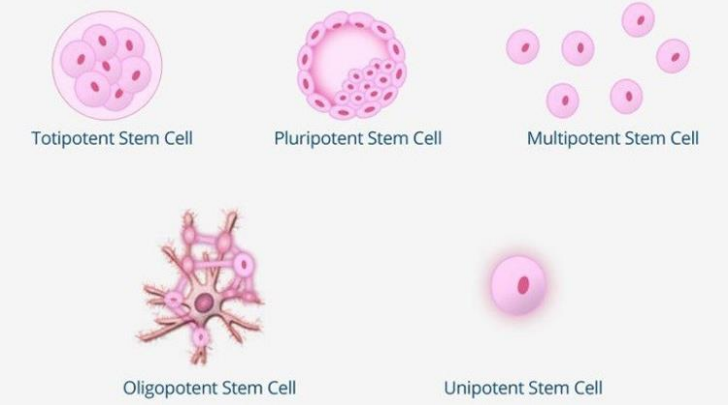

Image 1: Types of stem cells based on differentiation potency (Hildreth, 2022)

- **Totipotent stem cells** are able to multiply and specialise into various cell types within an organism as well as give rise to a fertile offspring (Ragab et al., 2017).
- **Pluripotent stem cells** are able to make every cell type except for cells found in the embryonic membrane (Barzegar et al., 2019).
- **Multipotent stem cells** have the ability to produce cells belonging to the same tissue they originate from (Ragab et al., 2017).
- **Unipotent stem cells** are capable of producing a single cell type while also having the ability to renew themselves (Kolios & Moodley, 2013).
- **Oligopotent stem cells** have the ability to develop into a limited number of cell types, such as myeloid or lymphoid stem cells (Cona, 2024).

Stem cells can have four potential outcomes on the basis of self-renewal and differentiation (Biehl & Russell, 2009). Multipotent stem cells, for instance, are able to be dormant, undergo asymmetric self-renewal, symmetric self-renewal, or produce two different kinds of

daughter cells (Biehl & Russell, 2009). These outcomes can affect the amount of stem cells required to produce particular cells and heal tissues (Biehl & Russell, 2009). Every outcome has a particular function to maintain the equilibrium of stem cells present inside the body (Biehl & Russell, 2009).

Stem cells possess mechanisms such as differentiation, neuroprotection, immunomodulation, and paracrine effects that play an important role in tissue repair and regeneration.

Differentiation

Stem cells can differentiate into various different cell types and tissues found in humans (Cona, 2021). Differentiation is the process in which stem cells develop into different types of cells that involve a transition from proliferation to specialisation (Tocris Bioscience, 2017). In cell differentiation, there are changes in morphology, metabolism, membrane potential, and response to signals that lead to specific cell functions and lineage (Tocris Bioscience, 2017). Signalling pathways such as the Apoptosis Signalling Pathway, MAPK Signalling Pathway, p53 Signalling Pathway, Notch Signalling Pathway, mTOR Signalling Pathway and changes in gene expression tightly regulate the stem cell differentiation process (Tocris Bioscience, 2017b). Growth factors, cytokines, and epigenetic processes regulate the differentiation of embryonic stem cells (ESCs) through signalling mechanisms. They are separated into two cells: a stem cell and a daughter cell, which will specialise. When daughter cells divide and differentiate, they ultimately mature into a specific cell type and cease dividing. Adult stem cells, conversely, are thought to be unspecialized and play a role in the upkeep and restoration of tissues (Tocris Bioscience, 2017). This process is important in stem cell therapy as it helps the cells develop into specific cells needed for body healing (Cona, 2021).

Neuroprotection

Neuroprotection involves strategies used to protect the central nervous system (CNS) from any harm caused by sudden injuries (such as stroke or trauma) and long-term neurodegenerative conditions (like Parkinson's, Dementia, Epilepsy, Alzheimer's, etc.) (Rehman et al., 2019). According to Amirbekyan et al. (2023), successful stem cell treatment for traumatic brain injury requires efficient stem cell transportation, movement, and integration to enhance neuroprotection. The study suggests that when human neural stem cells expressing L-myc are administered via the nasal route, they have a natural affinity towards the site of injury. These cells are thought to move to initial and subsequent injury sites, where they affect the biomarkers that are associated with nervous system protection and promote tissue recovery. Research conducted on rats with brain injuries indicated that when LMNSC008 cells are administered through the nose they migrate to injured areas and influence the gene expression associated with inflammation and tissue healing. The study suggests that the intranasal administration of LMNSC008 cells has the potential to treat traumatic brain injuries.

Immunomodulation

The immunomodulatory characteristic is the ability to regulate immune homeostasis in cases of excessive or insufficient immune response. Mesenchymal stem cells also have properties that allow them to regulate the immune system. The secretome of mesenchymal stem cells comprises cytokines, signalling molecules, chemokines, and growth factors, all of which play a significant role in immune and inflammatory response regulation (Huang et al., 2022). Immunomodulation of mesenchymal stem cells involves interactions with innate as well as adaptive immunity by directly interacting with the immune cells and secreting factors such as cytokines, chemokines, growth factors, and other

impactful substances (Huang et al., 2022). Previously conducted research suggests that mesenchymal stem cells primarily exert their immunomodulatory impact through the cytokines they secrete, but recent findings suggest that apoptotic and metabolically inactive mesenchymal stem cells also have immunomodulatory abilities, involving monocytes and regulatory T-cells (Song et al., 2020). In addition, modified and specialised mesenchymal stem cells can enhance the immunomodulatory effects for various medical uses (Huang et al., 2022). The versatile nature of mesenchymal stem cells allows them to serve as a promising treatment approach for immune disorders.

Paracrine effect

A recent study suggests that the positive impacts of stem cells might also be because of the paracrine effect (Baraniak & McDevitt, 2010). Paracrine signalling is a type of cell-to-cell communication where a cell releases a signal that causes neighbouring cells to change their behaviour or differentiation. The therapeutic effects of mesenchymal stem cell secretions, which consist of a wide range of molecules, cytokines, extracellular vesicles, chemokines, and growth factors that are involved in various biological processes, are known to have both local and distant impacts, referred to as paracrine properties (Ferraris, 2016). The paracrine factors secreted by stem cells cause the nearby cells to mature, influence processes in surrounding tissues, and affect the functions of the secreting stem cells, such as mesenchymal stem cells. These factors allow unidirectional communication between stem cells and more specialised cells (Ferraris, 2016). Those strategies that involve drugs, hypoxia, thermal shock, and pro-inflammatory cytokines have proven to be effective in improving the survival and paracrine functions of stem cells post-transplantation (Baraniak & McDevitt, 2010). Research is focused on comprehending and applying stem cell paracrine processes for tissue repair. Investigations are being conducted on the production of trophic factors, the impacts on regeneration and cancer treatments, and innovative approaches for regenerative medicine through the delivery of stem cell paracrine factors (Baraniak & McDevitt, 2010).

According to recent advancements, stem cells can be used for tissue regeneration and repair, gene therapy, genetic editing, drug discovery, drug testing, personalised medicine, disease modelling, and immunotherapy (Cona, 2021). The CRISPR/Cas9 system has revolutionised the field of stem cell research and demonstrated immense possibilities for practical use in regenerative medicine by modifying targeted genes in stem cells and then reinserting them into the patient's body to repair normal cell activity (Zhang et al., 2017; Cona, 2021). Furthermore, stem cells like pluripotent, foetal, or adult cells are used to form an organoid, a 3D tissue formed by self-organisation that imitates the important functional, structural, and biological aspects of an organ (Zhao, 2022). Moreover, bioengineered scaffolds along with stem cells are employed in direct transplantation in injured areas to repair the damaged areas and revive spinal cord or peripheral nerve function (Hong, 2022). Also, stem cells are utilised to create personalised therapies that match an individual's genetic and disease characteristics. They are also used to develop human tissue models for drug testing, which decreases the need for animal testing and offers a better understanding of how drugs interact with human cells (Cona, 2021).

Despite the substantial potential of stem cell therapy in treating different illnesses, the clinical application of stem cells in medicine brings up many ethical and safety issues (Cona, 2021). Critics claim the study is not ethical as it involves destroying the blastocyst, which is an unimplanted human embryo at the sixth to eighth day of development (Harvard

Stem Cell Institute, 2019). Currently, there are some concerns related to the use of induced pluripotent stem cells such as issues like consent of donors for the extraction of cells and the design of clinical trials, despite offering potential advantages for research (Railton & Sharon, 2019). Adult stem cells cannot be cultured for a longer period of time (University of Nebraska Medical Center, 2020). Also, it faces issues that need to be addressed such as immune system rejection, tumour development, and the requirement of a significant number of cells (Cona, 2021). Therefore, specific restrictions and regulations are applied to the studies that involve stem cells.

Regardless of the challenges, stem cell therapy holds a promising potential medical intervention for neurological disorders, given their ability to differentiate, replace or support damaged neural cells, exhibit the paracrine effect, modulate the immune response and also to repair and regenerate the damaged tissues.

Application of Stem Cell Therapy in Neurological Disorders

Neurological disorders impact the central and peripheral nervous system (World Health Organization, 2016). Stem cell therapy could be a promising medical intervention for neurological disorders like Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Spinal Cord Injuries, and Stroke.

Alzheimer's Disease

Alzheimer's disease is a progressive neurological condition involving brain changes, protein accumulation, shrinkage, and cell death, ultimately impairing memory, cognitive abilities, and basic task performance (National Institute on Aging, 2021) (Mayo Clinic Staff, 2023). It is classified as a neurological disorder because it affects some parts of the brain (CDC, 2021). According to the World Health Organization data, approximately 55 million individuals worldwide have dementia, with Alzheimer's disease contributing to 60-70% of cases (World Health Organization, 2023). The number of cases is expected to double in the future, thereby prompting an effective medical treatment for Alzheimer's Disease (Alzheimer's Disease International, 2024). According to Alzheimer's Disease International (2024), beta-amyloid proteins accumulate between neurons and form amyloid plaques due to the breakdown of the amyloid precursor protein. The beta-amyloid 42 type is especially damaging in Alzheimer's disease, as excessive amounts aggregate to interfere with cell function. Moreover, the tau protein forms neurofibrillary tangles within neurons in Alzheimer's disease. In normal neurons, tau helps to support microtubules, but in diseases, it separates and creates tangles that interfere with the function of neurons. There is evidence that suggests a connection between irregular tau, beta-amyloid, and additional elements that result in alterations in Alzheimer's brain. The irregular tau gathers in brain areas responsible for memory, while beta-amyloid forms plaques in the spaces between neurons. Once beta-amyloid levels hit a critical threshold, tau quickly spreads throughout the brain (National Institute on Aging, 2021). Furthermore, the loss of connections between neurons results in dysfunction of cells and atrophy of the brain. Neurons become damaged and no longer function properly, leading to the breakdown of networks and the shrinking of brain regions (National Institute on Aging, 2021). Only some types of neurons in particular areas of the brain are more susceptible. Gladstone Institutes conducted research that revealed the neurons containing elevated levels of apolipoprotein E are at a higher risk of degeneration because apoE regulates molecules associated with immune response (Stanley, 2021). Also, chronic inflammation can occur due to dysfunction of glial cells, particularly microglia, that do not effectively

remove waste and harmful proteins such as beta-amyloid plaques (National Institute on Aging, 2021). Stem cell therapy can be an option for treating Alzheimer's disease by repairing damaged brain tissue by differentiation, reducing inflammation, providing neuroprotection, promoting neuroplasticity and releasing growth factors to support the growth of new brain cells via paracrine signalling (Cona, 2021).

Parkinson's Disease

Parkinson's Disease is a progressive disorder that affects the nervous system and regions controlled by nerves, resulting in difficulties with movement, balance, coordination, cognition, senses, and emotional well-being (National Institute on Aging, 2022; Mayo Clinic, 2024). It is classified as a neurological disorder because it affects the nervous system. Parkinson's disease occurrence has increased, thereby resulting in a rise in the number of disability and death rates worldwide (World Health Organization, 2023b). Currently, Parkinson's Disease affects more than 10 million individuals (Parkinson's Foundation, 2024). The main reason for Parkinson's disease is the loss of dopaminergic neurons in the substantia nigra, a part that controls movement (Dauer & Przedborski, 2003). Furthermore, the absence of nerve endings responsible for producing norepinephrine, a chemical messenger found in the sympathetic nervous system, accounts for symptoms that are unrelated to movement such as irregular blood pressure, fatigue, and digestive problems (National Institute on Aging, 2022). The discovery of Parkinson's Disease genes suggests that accumulation of misfolded proteins and dysfunction in the ubiquitin-proteasome system play an important role in Parkinson's Disease development (Dauer & Przedborski, 2003). Mitochondrial dysfunction and oxidative stress also play a role in the accumulation of misfolded protein and damage to dopaminergic neurons. Neurotoxin-based models, especially 1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine (MPTP), have played a vital role in understanding the molecular process of cell death in dopaminergic neurons (Dauer & Przedborski, 2003). Scientists have discovered differences in the brains of people who have Parkinson's disease, such as the presence of Lewy bodies, which are microscopic markers of the disease. The Lewy bodies contain alpha-synuclein, a protein thought to be involved in the progression of Parkinson's disease. Researchers found grouped alpha-synuclein protein in the cerebrospinal fluid of people who later develop Parkinson's disease, leading to a strong emphasis on studying this in the scientific community (Mayo Clinic, 2024). Even though there are medicines like levodopa and carbidopa that are able to replace dopamine and ease symptoms, the permanent loss of neurons cannot be reversed (Ulrich, 2022). Therefore, stem cell therapy will be an efficient treatment as it can delay the advancement of Parkinson's disease and even reverse it, bringing it to a halt by repairing damaged neurons by differentiation, providing neuroprotection and promoting neuroplasticity.

Multiple Sclerosis

Multiple sclerosis (MS) is a condition of the central nervous system where the immune system attacks and damages the myelin sheaths covering nerve fibres resulting in chronic axonal loss (Podbielska et al., 2013). The observed symptoms are fatigue, vision issues, muscle weakness, numbness, clumsiness, bladder issues, dizziness, mood changes, and cognitive dysfunction (National Institute of Neurological Disorders and Stroke, 2023). It causes demyelination, inflammation, and neurodegeneration (Kurnellas et al., 2007). It is classified as a neurological disorder because it affects the central nervous system. According to the World Health Organisation, there are over 1.8 million people worldwide

who have Multiple Sclerosis (World Health Organization, 2023b). It is classified into four types: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS), each having distinct symptoms and progressions (Cleveland Clinic, n.d.). There is damage to the axons present in the central nervous system which are usually surrounded by myelin (white matter). It also affects the nerve cell bodies present in the grey matter of the brain and causes harm to the axons found in the brain, spinal cord, and optic nerves. The disease leads to the shrinking of the cerebral cortex through a process known as cortical atrophy (National Institute of Neurological Disorders and Stroke, 2023). Multiple Sclerosis causes the formation of scar tissue called plaques or lesions because of the immune system's attack on myelin (National Institute of Neurological Disorders and Stroke, 2023). Furthermore, NCX (Na+/Ca2+ exchanger) and PMCA2 (plasma-membrane Ca2+-ATPase 2) have been known to play a role in the dysfunction of axons and neurons in multiple sclerosis (Kurnellas et al., 2007). Preventing neurodegeneration by restoring their regular activity could possibly delay the progression of the disease (Kurnellas et al., 2007). Recently, it was found out that different types of T-cells (TH1, TH2, TH17, NKT, CD4+, CD8+, CD25+, T-regulatory cells) and B-cells engage in the peripheral and central nervous system thereby contributing to the pathogenesis of multiple sclerosis (Podbielska et al., 2013). Therefore, finding an effective medical intervention for Multiple Sclerosis is of utmost importance to avoid long-term disability, decrease the number and intensity of relapses, impede the progression of the disease, and improve the quality of life. Stem cell therapy can be a choice of treatment as it can replace or assist in the repair of cells that have been damaged, provide neuroprotection, and modulate the immune response.

Spinal Cord Injuries

Spinal cord injuries are caused because of damage to the spinal cord which is a long, delicate tube-like structure that originates at the base of the brain stem extending to the lower portion of the spine and the nerves at the end called the cauda equina (Mayo Clinic, 2023). The spinal cord transmits signals between the brain and body that affect the overall physical and emotional health of the person. More than 15 million individuals worldwide suffer from spinal cord injuries, predominantly caused by traumatic incidents such as accidents, falls and violence or by non-traumatic causes such as degenerative and vascular issues, tumours, toxins, infections, or congenital abnormalities (World Health Organization, 2024). Primary spinal cord injuries (SCI) occur when mechanical forces directly damage the cord, mostly due to trauma or compression caused by pathologies such as fractures or hematomas. Hyperextension injuries are caused by transient compression rather than impact. Some other mechanisms include distraction injuries from stretching and tearing and lacerations from sharp objects or dislocations (Bennett et al., 2020). Secondary spinal cord injuries are caused by biological processes that occur after the initial injury, including vascular damage, imbalances in ions, free-radical formation, inflammation, and excitotoxicity (Bennett et al., 2020). These injuries affect the vertebrae, disks, ligaments, or peripheral nerves, causing severe damage due to trauma, cancer, or infections (George, 2024). Severe injuries like dislocation or fractures of the vertebrae are caused because of accidents or altercations. These injuries result in debilitating and life-threatening secondary conditions and premature mortality (World Health Organization, 2024). Therefore, finding an effective medical intervention for spinal cord injuries is important to avoid long-term disability and improve the quality of life. Stem cell therapy can be a feasible option as it will provide neuroprotection, promote

neuroplasticity, replace damaged cells, and promote repair and regeneration.

Stroke

A stroke occurs when a blood vessel in the brain either ruptures or becomes obstructed, halting the flow of blood and oxygen, resulting in harm to the brain tissue and possible disability or death (Holland, 2018). Signs of a stroke include mild to severe weakness or paralysis on one side of the face or body, sudden headache, vision trouble, weakness, and speech issues (National Heart, Lung and Blood Institute, 2023). Stroke is classified as a neurological disorder as it affects the brain. According to a study report every year, 15 million individuals across the globe experience a stroke. Out of this number, 5 million people pass away while another 5 million are left with permanent disabilities (World Health Organization, 2022). Ischemic, hemorrhagic, and transient ischemic attacks are different stroke types, each having distinct causes and symptoms (Holland, 2018). Three main factors that lead to ischemic strokes are recognised: 50% result from arteriosclerotic plaques in cerebral vessels causing plaque rupture, 20% from cardiogenic cerebral infarction, and 25% from small vessel lesions causing Lacunar infarcts. Additionally, the remaining 5% can be attributed to other rare causes like vasculitis and extracranial arterial dissection (Zhao et al., 2021). Also, chronic inflammation is associated with ischemic strokes as it harms the blood vessels and leads to atherosclerosis (National Heart, Lung, and Blood Institute, 2023). A rapid onset of bleeding in the brain may result in a hemorrhagic stroke, which happens when an artery ruptures or releases blood. This causes swelling in the brain, increases pressure and harms brain cells. There are two kinds of hemorrhagic strokes: intracerebral haemorrhage (ICH), which happens in the skull, and subarachnoid haemorrhage (SAH), which occurs between the brain and its encasing membrane. In ICH stroke, the tissues surrounding the brain fill with blood due to a ruptured artery, whereas in SAH stroke, bleeding takes place between the brain and its covering tissues (Holland, 2018; National Heart, Lung, and Blood Institute, 2023). A transient ischemic attack, also called mini-strokes, is the result of a brain blockage that dissipates before leading to brain harm. They may only endure for under an hour before possibly evolving into a complete stroke (National Heart, Lung, and Blood Institute, 2023). Therefore, finding a medical intervention for stroke is of utmost importance to prevent disability and save lives. Using stem cell therapy for stroke can help prevent disability and save lives by replacing damaged brain tissue via differentiation, reducing inflammation, and promoting neurogenesis and neuroprotection.

Real Life Case Studies

Stem cell therapy has been shown to be an effective medical intervention for neurological disorders in various real-life cases.

Kristopher (Kris) Boesen

Kris Boesen's life took a drastic turn right before he turned 21 due to a car crash causing a cervical spine injury. The driver's loss of control on a wet road led to the car colliding with a tree and then with a telephone pole. At first, it was thought that Kris would be paralysed for the rest of their life as everything from his neck down was severed from his brain (Stem Cell Transplant Institute, 2020). Kris and his family faced the prospect of permanent paralysis until Asterias Biotherapeutics and CIRM offered hope through a stem cell trial. The trial involves a procedure for patients suffering from a spinal cord injury that aims to improve neurological function and restore the ability to use arms and hands, thereby potentially transforming patients' daily lives. The family were warned about the risk but they were hopeful for an improvement (Masatani,

2016). In order to be eligible for the trial, Kris had to fulfil certain criteria such as being between 18-69 years old, being 14-30 days post-injury, having a stable condition appropriate for AST-OPC1 injection, and being able to communicate once off the ventilator (Stem cells transplant institute, 2020). After Kris signed the consent forms, then they proceeded with the evaluations, imaging, and examinations (Stem Cell Transplant Institute, 2020).

A surgical team injected 10 million AST-OPC1 cells into Boesen's cervical spine with great care from Keck Hospital of USC. These cells are derived from human embryonic stem cells and are differentiated into oligodendrocyte progenitor cells (OPCs), which can be found in the brain and spinal cord. Basically, the AST-OPC1 aids in nerve regeneration through the production of neurotrophic factors, promoting vascularization, and initiating remyelination of exposed axons post-injury (Masatani, 2016). Almost six weeks later, he was released and sent back to Bakersfield to resume his recovery. Physicians checked his improvement after one week, a month, two months and three months following the injection, with more thorough evaluations scheduled for six months, nine months and twelve months (Masatani, 2016). Two weeks after the surgery, Kris noticed improvements. It was reported that Kris experienced a notable enhancement in his motor function, up to two spinal cord levels, as of 90 days after treatment. The person who couldn't do anything was able to feed himself, write, use his phone, operate his wheelchair, hug loved ones, and feel a better sensation in his upper body (Stem Cell Transplant Institute, 2020). This unforeseen development has inspired him to strive for greater self-reliance. Kris told Keck Medicine that all they had wanted from the start was an opportunity to fight. Kris remains optimistic about the possibility of recovering even more function. He said "If there is a possibility of me being able to walk again, then absolutely! I am willing to do everything in my power to accomplish that" (Masatani, 2016). Also, Rodney, Kris' father, was excited about Kris' advancements. He thought even if the progress halts at this point, Kris will still experience an improved quality of life with increased opportunities, especially because of the ability to use his hands which ensures a more promising future compared to before the surgery (McCormack, 2016).

Gordie Howe

Gordie Howe, a Canadian hockey legend was famous worldwide as "Mr. Hockey" and also known as "Mr. Stem Cell" (Schrotenboer, 2016). In 2014, Cathy Purnell discovered her father, Gordie Howe, on the floor in an unconscious state in Lubbock, Texas after suffering from a stroke at the age of 86. He struggled to speak and needed help to move as he was paralyzed from his right side. Despite the medical treatment, Howe's health continued to deteriorate. His memory deteriorated and he often expressed a desire to end his suffering. The family faced a tough time because of the decline of the once strong and spirited Howe as he became more dependent and lost his cognitive abilities (New York Magazine, 2015). In 2014, Dr. Maynard Howe and Dave McGuigan from Stemedica in San Diego reached out to Howe's family regarding a stem cell therapy experiment (Chan, 2016). This therapy required the injection of as many as 100 million neural stem cells into Howe's spinal cord. The objective was for the cells to travel to his brain, divide, substitute for those that have been damaged and help in the recovery of his brain. Stemedica claimed improvement within 24 hours and offered Howe the chance to join a stem cell trial for stroke patients. The therapy involved utilising bone marrow cells from a youthful donor and neural stem cells from foetal brain tissue, which is not authorised by the FDA (Chan, 2016). This prompted Howe

to travel to Tijuana, Mexico for treatment. The family was in consensus and journeyed to Clínica Santa Clarita for the stem cell injection. Howe got a stem cell injection in his spinal cord and regained his ability to walk after over a month. His family said that in a short period of time, he was walking without help, buying groceries, completing household tasks, and fishing. This progress prompted him to come back for another session in June 2015 in Tijuana (Chan, 2016). In May 2015, Murray Howe mentioned that his father showed no signs of having a stroke, but he admitted that his father had dementia and was experiencing a gradual deterioration in health (Schrotenboer, 2016).

While stem cell therapy is still in the clinical stages, there are more and more stories giving the medical community hope for a better, more definitive treatment for these medical conditions.

CONCLUSION

Neurological disorders affect the central and peripheral nervous system causing cognitive difficulties, vision and speech problems, and involuntary movements. The prevalence of these disorders has increased worldwide. It is suggested that the numbers are going to double in the future. Neurological disorders have a detrimental effect on not just the individual and their family, but also on communities and economies, emphasising the importance of addressing them. This paper examines the potential of stem cell therapy in treating neurological conditions such as Alzheimer's, Parkinson's, Multiple Sclerosis, Spinal cord injuries, and Stroke.

Stem cells have properties such as self-replication, differentiation, and plasticity which allow them to carry out various tasks such as maintaining tissues, regenerating tissues, and repairing injuries. They can be classified based on their differentiation potency, which includes totipotent, pluripotent, multipotent, unipotent, and oligopotent stem cells, as well as based on their origin, including embryonic stem cells, adult stem cells, induced pluripotent stem cells. Stem cells that have the ability to renew themselves and differentiate can have four possible outcomes: becoming dormant, undergoing symmetrical self-renewal, undergoing asymmetrical self-renewal, or producing two daughter cells. Differentiation, which is the potential to evolve into various cell types, neuroprotection, which involves strategies to protect the central nervous system, immune modulation, which is the ability to regulate immune balance in cases of overactive or underactive immune responses, and paracrine signalling, a way for cells to communicate with each other by releasing signals that prompt neighbouring cells to alter their behaviour or specialise, are the ways in which stem cells can assist in repairing and regenerating tissues. However, despite its potential as a medical treatment, it encounters ethical issues such as the destruction of embryos, concerns about donor consent, and issues with clinical study design. Challenges include the risk of tumours, immune rejection, the need for a large number of cells, and limitations in cultivating adult stem cells for long periods.

That being said, stem cell therapy can be a choice of medical intervention for neurological disorders such as Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Spinal Cord Injuries, and Stroke by replacing damaged brain tissue via differentiation, promoting repair and regeneration, modulating the immune response, releasing growth factors to support the growth of new brain cells via paracrine signalling and promoting neurogenesis, neuroplasticity, and neuroprotection. Stem cell therapy has the potential to avoid long-term disability, decrease the number and intensity of relapses of a disease, impede the progression of the disease, and most importantly save lives and improve the quality of life. It is a promising

medical intervention in the field of medicine and proves to be effective in various real-life cases as seen in Kris Boesen and Gordie Howe's case.

Currently, stem cell therapy research is rapidly progressing and has reached clinical trial stage despite the challenges it faces, but it will soon be ready for implementation. In the coming years, stem cell therapy is expected to have a significant and positive impact on the medical sector and, consequently, on human health.

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