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Abstract

Multiple Sclerosis (MS) is a neurological disorder that affects about one million people in the United States. The disease results from an abnormal immune response where T cells damage the myelin sheath in the central nervous system, causing scarring. The lesions can occur in any part of the brain or spinal cord, and thus affects every patient differently. One of the most detrimental effects the disease has on patients' lives is the decreased ability to walk. There has been research and treatments to manage pain and slow progression of the disease, but little progress has been made to enable MS patients to walk more comfortably. Previously, there have been gait training devices in use. However, many require intensive manual labor which causes the patient and the physical therapist to fatigue easily. Recently, Ekso, a self-supporting robotic exoskeleton, designed for patients with spinal cord damage, has been shown to improve gait and overall quality of life in patients with MS.

Introduction

Multiple Sclerosis is a degenerative neurological disease affecting the Central Nervous System. Unfortunately, it affects many younger people, mostly diagnosed in women between the ages of 20 and 50. There is often physical and emotional pain associated with the disease. There are various medications in use that can treat those symptoms and help improve the patients' quality of life (Ziemssen, 2011). However, change in natural gait is a consequence of MS that disrupts patients' daily lives. Over time, a patient's ability to walk deteriorates. Progressive worsening of gait is self-reported and is also demonstrated through data measured on various scales by researchers (Motl, et al., 2018). Robotic exoskeletons have been shown as an effective way to retrain gait. Exoskeletons are designed to mimic the movements of human limbs. They attach to the extremities and can control the position and alignment of the joints. Exoskeletons can also be programmed to provide support based on the patient's motor capabilities (Iandolo, et al., 2019). This paper discusses the pathology and musculoskeletal effects of MS and examines the effectiveness of robotic exoskeletons in improving gait of MS patients.

Methods

The information in this review is collected from various academic and scientific articles obtained from the EBSCO, PubMed, and ProQuest databases accessed through the Touro College library. Each article was analyzed in order to determine its relevance to the thesis.

Discussion:

Glial Cells and the Myelin Sheath

The nervous system is made of separate parts that work in tandem. Included is the central and peripheral nervous systems. The central nervous system is made up of the brain and spinal cord while the peripheral nervous system is composed of the nerves that connect the CNS to the rest of the body. Although they are not neurons, glia are a fundamental component of the nervous system. The glial cells espouse the neurons and enable them to function properly. Astrocytes are the most common type of glial cell. Astrocytes fill the spaces between neurons, providing support. Astrocytes also contribute to the maintenance of the chemical balance in the neuron by controlling the extracellular chemical concentration and assisting in the reuptake of neurotransmitters. There are also microglia that are involved in removing debris in the nervous system, ensuring that messages can travel without blockage. Another type of glial cell is myelinating glia. Myelinating glia are divided into two subtypes, oligodendrocytes and Schwann cells. Oligodendrocytes are in the central nervous system, while Schwann cells are present in the peripheral nervous system. These cells provide insulation to the neurons by wrapping around their axons in a covering known as myelin, forming the myelin sheath. Myelin provides insulation, allowing signals to be transported faster. There are small gaps in the myelin sheath known as nodes of Ranvier. When an action potential moves down an axon it is regenerated at the node of Ranvier in a process known as saltatory conduction (Bear, et al., 1996).

Pathology of MS

Multiple Sclerosis is a condition where the body's immune system attacks the myelin sheath. MS usually presents at first with an attack that lasts between a few days and a few weeks. It is followed by a period of relief that can last from a few months to a few years. The reprieve is a result of an autoimmune reaction. This mild form of MS usually lasts for about ten years, but varies by case. As the disease progresses, the attacks become less distinct, and the patient's condition greatly deteriorates. During the later stages of the disease, the underlying axon is damaged in addition to the myelin sheath. The axon loss in the spinal cord causes spinal cord atrophy which can make it difficult for the patient to walk and lead to paralysis (Lucchinetti, et al., 1996).

Many protein sequences on the myelin sheath are similar to microbial protein sequences. As a result, the immune system attacks the myelin in a process known as molecular mimicry. Many relapses of MS occur as a result of infection from a virus. Herpesvirus 6, influenza, measles, papilloma virus, and Epstein-Barr virus all have gene encoding sequences that are similar to the main protein structures of the myelin. Antibodies bind to the myelin instead of the microbe. If a T-cell or B-cell is activated by the microbe, it can penetrate the blood-brain barrier (Steinman, 2001).

The diagnosis of MS is a complex process and multiple factors need to be taken into account. Firstly, there need to be lesions in the white matter of two separate parts of the CNS that developed at least a month apart from each other. All other neurological disorders with similar symptoms need to be ruled out. In addition, an MRI must be performed. The MRI will display the lesions and successive MRI scans can be a tool to help the physician track the progression of the disease. It also needs to be determined that the CNS is chronically inflamed, which can be assessed by a spinal tap. A spinal tap allows the physician to see if there are oligoclonal bands in the fluid which indicate neurological disorders. In addition, each episode of attacks needs to be distinct and last for 24 hours or more. As the disease progresses, it can be subcategorized (Garg, Smith, 2015).

MS affects the myelin of the CNS. Each part of the brain and spinal cord control different neurological functions, so the effects of the lesions can manifest in different ways. Relapsing–remitting MS is the most common form of MS. The person will have separate attacks that can last from a few days to a few months. In between attacks, there is a period of reprieve where symptoms get better and there is no neurological degeneration. The next type of MS is Secondary Progressive MS (SPMS). In a patient with SPMS, the condition worsens gradually with time and the patient does not experience any episodes of relief. Primary progressive MS (PPMS) affects a minority of MS patients. It is characterized by an unrelenting decline in neurological function. There are no relapses or remissions, but there are occasional periods where there is no significant deterioration. Lastly is progressive-relapsing MS (PRMS). PRMS is the rarest form of MS. From the beginning of PRMS, the symptoms get progressively worse. However, it is different from other types of MS because there are periods where the attacks are more intense and debilitating with no periods of remission (Loma, Heyman, 2011).

In the worst stages of MS, there are no phases of relief, as there is destruction to the axons and atrophy of the brain and spinal cord. AMPA is an ionotropic transmembrane receptor for glutamate that allows for fast synaptic transmission in the central nervous system. AMPA receptors are present on oligodendrocytes. During an MS attack, lymphocytes, brain microglia and macrophages release large amounts of glutamate, which activate the AMPA receptors and cause overstimulation. However, if the receptors are blocked, it can mitigate some of the damage from the glutamate. AMPA is not involved in the immune response, but it can protect the oligodendrocytes from being damaged. Medications that block glutamate receptors are being utilized to treat this aspect of MS (Steinman, 2001).

The Effect of MS on Gait

Since MS affects the spinal cord, the main support of the body, a patient's gait can be affected, causing difficulty walking. Damage to certain areas of the spinal cord can lead to muscle spasticity. Muscle spasticity is an increase in rigidity of the muscles. The stiffness can be mild or it can cause involuntary uncontrolled movements of the extremities. The stiffness can make straight limbs hard to bend or bent limbs hard to straighten. Since many MS patients suffer from fatigue, extreme tiredness can make coordinating movement challenging. MS patients can also suffer from weakness in the leg muscles, altering normal stride. The change in walking pattern can cause pain, furthering the difficulty of walking (nationalmssociety.org).

MS patients can also suffer from balance issues, affecting their ability to walk properly. The balance issues can be caused by many different factors, such as vision and sensory issues. A patient may have reduced visual acuity or lack proper depth perception. This can be hazardous to a patient because it affects their ability to be aware of their surroundings. MS-related sensory issues can cause numbness which results from reduced muscle spindle and joint receptor activity. This can lead to decreased sensation in the feet which compromises stability and makes it difficult to navigate uneven surfaces. There is also the vestibular impact of MS on balance. The vestibulocochlear nerve is responsible for both hearing and balance. In MS patients, the vestibulo-ocular reflex is reduced, affecting the ability to stabilize gaze, causing dizziness and unsteadiness (nationalmssociety.org).

Motor systems can also be affected by MS. Patients with MS often have decreased muscle strength and endurance. This makes it difficult for patients to use a wheelchair or scooter on their own. There are also issues with muscle control and range of motion. This can lead to an inability to anticipate changes in the environment, resulting in an increased response time. Patients may also over or under compensate with other muscles in order to make up for the decreased function. These issues can lead to uneven gait (nationalmssociety.org).

Neurological Impact of MS on Gait

A study was done with patients in the early stages of MS to assess the way gait is affected by neurological deficits. Depending on how the gait and neurological systems are impaired, gait patterns will be different among patients and even differ in the same patient over time. Disturbance of normal gait is reported as the most debilitating symptom by MS patients. The gait of MS patients was compared to a control group of healthy people. MS patients walked slower and used shorter steps. In addition to walking less efficiently overall, there was a decrease in velocity and stride length over the course of the day as the patients became more fatigued. The patients in the study were scored on the Expanded Disability Status Scale (EDSS) scale by a neurologist. The EDSS scale measures neurological disability by assessing motor, sensory, cerebellar, brain stem, visual, and mental abilities. Gait was measured using the GAITRite Analysis System, a computerized mat with sensors that measured contact of the feet with the mat. The system combined the time and distance into a score known as the Functional Ambulation Performance (FAP) score. The system removed points for dysfunction of each leg, lack of lower limb strength, and the use of assistive devices. The FAP score was highly correlated with neurological abilities. The more neurological impairments a patient had, the less efficient their gait. The data also suggests that the impairments in upper motor neuron function lead to abnormal gait in MS. Significant changes to the FAP score would suggest a relapse in the MS (Givon, et al., 2009).

Gait Training

Conventional physical therapy involves different techniques that help patients improve gait and reduce the risk of falls. Treatment for MS involves stretching to reduce spasticity of the muscles and maintain the patient's range of motion at the joints. Exercises also work toward improving trunk control and increasing strength in the upper arms. Physical therapists also teach MS patients how to adapt to the environment and use aids such as wheelchairs and braces (Schwartz et al., 2011).

Physical therapists work with patients on balance exercises as well as strength and resistance training. In the past, Bodyweight-supported treadmill training (BWSTT) was a popular method to improve gait in patients with MS. BWSTT is based on the effectiveness of intensive and task-specific gait training. The user wears a harness which is held up and supported by the therapist. The patient has minimal support from a rope attached to the harness and walks on a treadmill, while the legs are physically guided by the therapist. However, this is extremely exhausting for both the patient and the therapist. It is also impractical for patients that have limited function of their legs (van Kammen, et al., 2016).

A study compared walking on a treadmill regularly to walking on a treadmill with body weight support in 10 healthy individuals. Normal gait pattern was disrupted when body weight support was provided. In addition, neuromuscular control of walking was affected. As gait speed increased, the differences between walking with and without support were less pronounced. It was recommended that higher speeds and less bodyweight support should be provided to patients when trying to reinstate a natural gait (van Kammen, et al., 2014).

Recently, robot-assisted gait training devices have been recognized for their ability to provide walking assistance to patients with severe gait disabilities. The robots, also known as exoskeletons, allow the patient to walk on flat ground. The parts of the exoskeleton that attach to the lower extremities are connected to a computer. The physical therapist can use the software to manually adjust the angles of the different parts in order to mimic the ideal gait of the specific patient (Berriozabalgoitia, et al., 2021).

What is Ekso?

The Ekso is a robotic exoskeleton developed by Ekso Bionics in Richmond, California. The Ekso is made of carbon fibers and steel. It functions as an exoskeleton by attaching to the thigh, lower leg, and foot. The sensors embedded in the attachments respond to input from the user's muscles. A backpack that is worn to support the torso (Lajeunesse, et al., 2015). There are motors located at the knees and hips. A spring-loaded footplate ensures that the patient's steps clear the floor. The device supports itself and does not add any additional weight to the user. The user may require the assistance of a gait aid such as a walker or cane at first, but eventually many patients can walk on their own. The advanced software allows the physical therapist to set the parameters for the level of assistance that the robot provides, including the areas of step height, step length, and swing speed. The purpose of this is to promote participation from the patient in a way that is reasonably challenging (Wee, et al., 2020).

There are three levels of assistance that the Ekso software can provide. The lowest level, named FirstStep, requires the physical therapist to initiate the step using a controller. The patient is not involved in initiating the movement. This is often used in the beginning stages of treatment when the patient is learning to use the device. In ActiveStep, the patient presses a button and the device initiates a step forward. The most advanced level is ProStep, where the device moves when the patient engages in normal walking behavior such as lifting the foot and shifting the weight forward. The Ekso is highly beneficial because it can be programmed to work with patients that have mild to severe gait issues (Thomassen et al., 2019).

A main goal of physical therapy in neurologically impaired patients is to recover gait. Walking is important for physical and mental wellbeing. The best outcome is based on the principles of relative and repetitive training. The Ekso is relative because it allows the patient to experience a real walking position. It can be used in both indoor and outdoor environments. The Ekso training is repetitive because the patient spends multiple sessions walking wearing the device. Exercise that is high-intensity and is task-specific has been shown to promote the most progress toward recovery (Russo, et al., 2021).

Gross Motor Improvements

The trunk muscles are an integral part of maintaining proper posture during sitting and standing. Proper posture is also the first step in achieving a normal gait. Trunk muscles are activated systematically during walking to keep the body steady. Faster gait speed requires higher levels of trunk muscle engagement to keep the body stable. Engaging the trunk muscles to improve trunk function can provide many rehabilitative benefits. As opposed to other exoskeleton devices, Ekso requires the user to initiate the stepping movement by shifting their weight. This requires full body weight-bearing, which forces the user to activate their trunk muscles. Usage of the Ekso showed an increase in trunk activity both in the anterior-posterior and medial-lateral directions. The level of trunk muscle activation was much higher with the Ekso than voluntarily induced contraction. Research also suggested that the voluntary stepping promoted activity in the cortical and vestibulospinal pathways which shows the Ekso can promote neuromuscular improvement (Alamro, et al., 2018).

A study was done with 36 MS patients that required assistance when walking outside. Both the control group and the intervention group participated in weekly sessions with a physical therapist. However, the intervention group engaged in biweekly training with a robotic exoskeleton for three months. The parameters of the exoskeleton were set according to each individual patient's motor skills and joint mobility. The length of the sessions increased as time progressed, and endurance improved. The sessions were stopped early if the patient requested or if the physical therapist noticed signs of fatigue such as increased muscle tone and stumbling. At the end of each session cooling therapies were used on knee extensors and ankle plantar flexors to prevent exercise-induced hyperthermia and muscle fatigue. The study displayed that robotic gait training in addition to regular rehab sessions preserves gait speed and improves functional mobility in patients with MS. The exoskeleton did not cause increased fatigue in the participants. The control group showed an overall decline in physical function. The effects were two-fold as the symptoms did not improve, and the disease got progressively worse. The Ekso exoskeleton is a crucial tool in rehabilitation because it encourages cognitive control of body movements, specifically in the area of weight shift (Berriozabalgoitia, et al., 2021).

Quality of Life Improvements

A robotic exoskeleton can also improve the quality of life in patients with MS. The exoskeleton provides a highly repetitive and intensive gait training experience. The user is held in an upright position while walking around. The exoskeleton is portable, which allows it to be used in any environment, including outdoors. This is engaging and rewarding to the patient to be able to experience walking in a way very similar to a healthy individual. A study was done with a 51-year-old non-ambulatory patient. The goal for this patient was for her to be able to assist in transfers, to reduce the burden on her caregivers, and to improve her quality of life. Compared to other studies, the purpose here was not to promote ambulation. The patient used the Ekso robotic exoskeleton for a total of 15 sessions that occurred for one hour twice a week. The distance covered during each session was dependent on the patient's level of fatigue. After the Ekso sessions, the patient showed an increase in right knee extensor strength which made the sitting to standing transition easier. As the therapy progressed, the patient's endurance increased as well, and she was able to walk further distances. There was no change in spasticity, trunk control, or balance. However, the most notable improvement was in the patient's quality of life. Prior to using the exoskeleton, the patient was depressed and did not want to participate in social activities. After treatment, the patient expressed to the researchers how her self-confidence and self-esteem improved (Wee, et al., 2020).

Patients with impaired walking function are often confined to wheelchairs. However, wheelchairs do not promote muscle movement and can lead to muscle atrophy. In addition, the patient sitting in the wheelchair is lower than everyone that is standing, leading to feelings of inferiority. Participants reported feeling free and independent when using the Ekso. Additionally, patients that required walking aids such as a walker or a cane had previously felt unsteady while walking and feared falling. While using the Ekso, they felt supported and secure, so they were able to focus on the actual leg movement (Thomassen et al., 2019).

Conclusion

The impairment of gait is reported as the most debilitating symptom of MS. Although many gait training methods have been used over the years, few have led to significant improvements. Ekso is a new robotic exoskeleton that has recently been trialed for its effectiveness in improving the gait of MS patients. Studies have shown that using Ekso, patients' gait and quality of life has improved. There is hope that the Ekso will become more widely available in order to provide more patients with the euphoric experience of walking again.

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