Introduction

To date there is little to no reliable treatment for demyelinating diseases. Multiple Sclerosis or MS is the most prevalent of such diseases, inducing a variety of neurologic deficits ranging from pain to most notably difficulty walking. Due to its subjective nature, MS is difficult to give a definite diagnosis as patients interpret symptoms differently in various presentations. Symptoms are also not always active, putting a time limit on being seen for such disabilities and the formation of a diagnostic plan. While definite signs of MS do exist in notable damage to the myelin sheaths that envelope the axons of neurons, the justification for an MRI confirmation is not strong over subjective and ambiguous complaints of patients. Not only are symptoms waxing and waning but symptoms such as generalized pain don't necessarily offer guidance as to which region of nerves may be damaged. Even when properly diagnosed, there is very limited treatment available for MS, none of which promise overwhelming abatement of symptoms or treatment of the underlying problem. Many drugs currently used to treat MS are reliant on the prognosis or severity of the disease, which as stated previously is easier said than done.

Purpose of the Study

The purpose of this study is to have more clearly defined parameters for diagnosing multiple sclerosis. Along with diagnosis is a more appropriate and streamlined treatment plan for those who present with MS. Secondly is a theoretical proposal for a new treatment for MS and demyelinating diseases, including trauma cases, in which artificial myelin is introduced to the neuron to promote conduction and natural re-myelination.

Abstract

MS is the cause of many major deficits which impact millions of people in their daily lives. With more severe symptoms, it can take away a person's ability to ambulate unassisted and continue to progress into a potentially life-threatening disease. More severe forms may be comorbidity with higher levels of cardiovascular disease as well as increased infection rates (Manouchehrinia et al. 2016). Life expectancy for someone diagnosed with MS is reduced by 7-13 years (Scalfari et al 2013). This is a disease that progresses over the course of a patient's life, often taking several years to make the jump from one stage to the next (Tremlett et al. 2006). The jump from stage to stage however, is inconsistent and case based, using disability scores as guidance (Koch M et al 2009), (Confavreux et al. 2000), (Pittock et al 2004), (Tremlett et al 2006), (Koch et al. 2010). The early detection and diagnosis of MS is important when combating and categorizing its effects. There is a correlation between more frequent episodes earlier on in disease prognosis, with more frequent events early on hinting towards secondary progression (Vollmer 2007), (Eriksson et al. 2003), (Ebers 2005), (Scalfariet al. 2010). Current treatments of the various severities of the disease are scarce and often have their own detriments. Thus, it is important to find alternatives that will show promising efficacy as well as safety.

Along with the identification of disease progression, a new technique for treatment is needed. Proposed is the idea of physically repairing traumatic or degenerative myelin sheaths, replacing them with artificial scaffolds that will bind to the nerve and coat it; providing the electrical and protective insulation needed to carry out the functionality of the nerve.

Background

Multiple Sclerosis is defined by the damage to or break down of a myelin sheath around and axon. Once compromised, a neuron is susceptible to further degradation or inflammation. MS has many different pathologies which range from benign to severe. They can have etiologies ranging from trauma to autoimmune disorders. Symptoms are most frequently waxing and waning, with more severe status occurring more frequently. Severity of deficit is typically measured using a 10-point scaling system, 0 meaning asymptomatic MS and 10 meaning cause of death (Kurtzke 1983). This scale is widely accepted as a more standardized way of testing otherwise subjective findings; a rating of 6 on the expanded disability status scale or EDSS for example, indicates a major benchmark that the patient must have assistance when walking.

Identifying MS appears as cerebral lesions or lesions covering the spinal cord on MRI. There has been a focus on identifying signs and symptoms of MS at early stages in order to begin early treatment but more importantly to monitor the progression of disease; however, there is no way to accurately predict timing of episodes (Swanton et al 2014). While data is limited, findings suggest that rate of progression of lesions can lend a hand in determining disease prognosis. Prognosis is classified in two major categories, progressive and relapsing-remitting. Each major category has several subcategories dependent on severity and pattern of flare ups. While rapid MRI changes may hint towards a more aggressive form of MS, it is not indicative of what form or category is being seen. As such, categorization of MS is always a retroactive prospect based off a combination of MRI lesion load, timing/severity of symptom flare ups, and an EDSS score.

Difficulties lie with accumulating accurate data when it comes to MS. Many patients may experience their first episode but have minor symptoms and never get seen by a medical professional for what is a form of MS. Furthermore, MS is often overlooked when in combination with comorbidities. Cause of death from MS is also largely underrated as MRI tests are less frequent on deceased patients.

Conclusion

Using microscopic three-dimensional printing techniques, a bioscaffolds will be printed using bio-compatible materials. These scaffolds will allow for neuronal conduction, insulate the nerve, and provide a sturdy and flexible backbone to the nerve. This will effectively repair the nerve, while it regains functionality naturally through induced re-myelination. Some drawbacks of such treatment are the administration of the drug. It requires injection at a very precise and small scale over delicate nerves and would require a skilled administrator.

Future studies may consider smaller administration as new techniques and technology are available; repair of smaller peripheral nerves may become possible. Other areas would include administration in the brain itself.

Alternate uses and applications may be to enhance reaction time and signal induction using a better insulated material that allows for quicker transmission over a nerve.

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Artificial Myelination

Method

To treat degradation or traumatic injury of nerves and their myelin sheathes, A three-dimensional printed scaffolding of bifunctional molecules would be implanted over the existing damage in order to repair the defect. Due to the invasive nature of coating this scaffolding onto a nerve, treatment will always be retrospective instead of prophylactic. The scaffold would be composed of materials that support mechanical function and neuronal malleability using techniques developed by Arinzeh et al. (2017) to make the electrical conducting scaffold on a microscopic scale. The scaffold is made of a ceramic and polymer material that would encapsulate the neuron, providing insulation and improved conduction of the cell, restoring its ability to send electrical signals throughout the body. The immediate treatment would restore function to the cell however; the scaffold would be coated with neurilemmal cell differentiation promoting material that induces a natural re-absorption of myelin by the body. Cell activation will be attenuated by the scaffolding which will provide the necessary insulation and conductivity for the neuron to function normally. It will be layered as that of the natural myelin, with the artificial sheath being laid on top of itself in a spiral formation over the axon of the nerve, which will maximize the surface area and insulation.

Along with the use of artificial myelin sheaths, would be the use of more frequent MRI studies. These prospective studies should clarify the different features between benign, relapsing remitting, and progressive disease (Rovaris et al. 2009). New MRI findings lend insight to the development and progression of disease worsening which would be used to qualify a patient for treatment with artificial myelination implants. Patients would be screened by severity of deficit and MRI lesion load to qualify for treatment. Patients complaining of recurrent headaches or body aches; those who see their PCP or are in the hospital three or more times within seven years, with MRI findings consistent with multiple sclerosis will be monitored as potential recipients of treatment. Once qualified, patients should be followed up on annually for continued MRI studies in order to determine a progressive prognosis. With worsening of lesion load and an EDSS of 6 or greater a patient would qualify for this procedure. Strict prerequisites are a product of the invasive nature of the procedure. Artificial sheaths will be assembled based off severity of nerve damage, with areas of higher lesion load requiring thicker insulation.

Scaffolds are made with a three-dimensional printing method to a diameter as small as 5 micrometers using functional polymers. Treatment depends on an EDSS of 6 or more with consideration for MRI lesion load. Basing the thickness of the artificial myelin sheath on the damage done to the nerve will allow for a consistent diameter across nerves. The scaffold is embedded in a solvent of N-dimethylformamide and will be administered via injection over the areas of the spinal cord and large peripheral nerves to maintain a smooth surface (Arinzeh et al 2017). Symptoms will be instantly reversed, restoring full functionality of the effected nerves. This will Allow for the patient to resume their normal lifestyle as in the short term as well as promote aggregation and reuptake of myelin, restoring functionality long term.

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