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Case Report

# Functional Neuroprostheses for Foot Drop Improve Gait Outcomes in Primary Lateral Sclerosis

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## Abstract

Functional neuroprostheses deliver electrical current to induce muscle contraction to help improve limb clearance issues. These technologies have been applied to several neurologic disorders, but their role in primary lateral sclerosis has not been investigated. This case presents the results of bilateral neuroprostheses employed to improve gait mechanics in a 51 year-old male patient with lower extremity spasticity due to primary lateral sclerosis. The patient's gait and balance were evaluated with and without functional peroneal nerve stimulation. With functional electrical stimulation, the patient improved in four separate measures of gait function: gait velocity (0.73 m/s vs. 1.0 m/s), distance traveled in 6 minutes (281.6 m vs. 376.1 m), the "Timed Up & Go" test (22.51 s vs. 14.01 s), and the functional gait assessment (10/30 vs. 22/30). This case report provides insight into the efficacy of neuroprostheses in the management of lower limb spasticity in patients with this disease.

## Introduction

Primary Lateral Sclerosis (PLS) is a progressive disorder of the upper motor neurons, with a majority of patients suffering from lower extremity impairment [1]. Most patients first present with leg symptoms [2], with weakness, spasticity, or ambulation difficulties among the most common [3]. PLS is generally considered less severe than Amyotrophic Lateral Sclerosis (ALS). Patients with PLS do usually live longer than those with ALS, though they may become just as disabled [2]. The pathophysiology of PLS remains unclear.

Foot drop is a common cause of difficulty walking in patients afflicted by neurologic illness. To achieve a more natural heel-strike, the passive Ankle-Foot Orthosis (AFO) is commonly used and has been specifically shown to improve gait speed in patients suffering from chronic hemiparesis and stroke [4,5]. 'These devices' relatively low cost and compact design have made them a workhorse for the management of foot drop, yet their restriction of motion and inability to assist in the propulsive component of gait have led researchers to develop active orthoses, including the quite modern class of neuroprostheses [6].

Neuroprostheses represent a modern approach to improving the lives of patients with muscle weakness. Their use has been studied in the treatment of a variety of neurologic disorders, including stroke, spinal cord injury, multiple sclerosis, and familial spastic paraparesis [7]. These devices use Functional Electrical Stimulation (FES) to activate the firing of intact lower motor neurons to achieve muscular contraction. Foot drop is the most common clinical indication for these neuroprostheses that deliver an electrical current to the peroneal nerve to stimulate foot dorsiflexion. With regard to improving ambulation, these devices have the most studied tenure within stroke patients, with moderate improvements seen during acute rehabilitation [8] and significant increases in gait speed observed over the long term [9]. In studies of patients with chronic hemiparesis and foot drop, FES significantly improved gait measurements [10] as well as functional ability and participation in community life [11].

Neuroprostheses have been applied to patients with a variety of disorders, including neuromuscular diseases, yet the outcomes of this technology in those with PLS have yet to be investigated. Since PLS is a progressive disease, we were especially interested in learning this technology would perform over time. Here we describe the effects of FES in a patient with PLS over 2 years of follow up.

## Patient and Intervention

The patient is a 53 year-old male who began to notice symptoms 16 years prior. He first began experiencing what he described as "pseudobulbar affect," which manifested as unintended crying or laughter. One year later he noticed a twitching sensation in his limbs and subsequently developed bilateral foot drop. Two years later he developed dysarthria and excessive salivation. The patient's ambulation worsened, necessitating a use of a cane. By the time the patient presented to our clinic at age 47, he had suffered multiple fractures after several falls, including a right radius fracture, two separate rib fractures, an acromioclavicular joint injury, a left thumb CMC ligament tear and exam findings of a C5-C6 compression fracture. His workup began at an outside facility. To exclude mass lesions or demyelinating disease, he had undergone MRI scans of his brain and entire spinal cord, which were unremarkable. To exclude ALS, he had undergone an EMG, which demonstrated trace insertional activities in some of his upper extremity and lower extremity muscles with the majority of assessed muscles showing no abnormalities. The patient's family history included multiple relatives of both genders who developed "leg clumsiness" and stiffness in their late 40s. His physical exam revealed spasticity in all limbs with the lower extremities more severely affected, as well as brisk reflexes and palmomental, Hoffman's and Babinski signs. Muscle strength was full but the examiner noted difficulty assessing this with the background spasticity. His sensation was intact throughout. To exclude metabolic

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causes of upper motor neuron dysfunction we performed serologic studies of B12, E, and copper, and these were all within normal limits. The two most likely diagnoses were PLS and Hereditary Spastic Paraparesis (HSP). The strong family history supported HSP, while the prominent bulbar symptoms, lack of urinary urgency or impaired vibration sensation bolstered a PLS diagnosis. These subtle clinical clues have been used to differentiate the two [12], yet genetic testing remains a superior tool [13]. Subsequent genetic testing for common HSP variants did not reveal any clinically relevant mutations, and thus a verdict of PLS was reached.

Over the next three years, multiple interventions were employed. The patient had already tried oral baclofen and diazepam with limited success. Amitriptyline was added to address his chief complaint of pseudobulbar affect. Levetiracetam was added for his muscle cramping and diazepam was later replaced with clonazepam. Three years after presenting to our clinic, the patient had an intrathecal baclofen pump placed. This improved his speech but only provided a limited improvement in his lower extremity spasticity.

Physical therapy educated and instructed the patient in common spasticity management techniques including lower extremity stretches for hip flexors, hamstrings, and gastrocnemii. He was provided with trunk rotation exercises and encouraged to perform stationary cycling and to exercise in a warm-water pool. He had a trial with over-the-counter posterior leaf spring braces (flexible AFOs), which improved limb clearance to a small extent, and it was recommended that he use a cane (initially) and later a rollator walker due to the frequency and serious nature of his falls. The patient did not use the braces or the rollator walker on a regular basis as he felt it impeded his function. He continued to fall and just prior to a neuroprosthesis trial, he reported a frequency of ~10 falls per year.

Later that year, at age 51, the patient completed three trials using bilateral neuroprostheses, specifically the NESS L300, over a three-month period. The NESS L300 uses a gait sensor to detect the force under the foot in order to determine swing and stance phases of walking. During swing phase, the gait transmitter uses radio frequency signals to communicate with a control unit. This unit then directs a hybrid orthosis with an integrated stimulation unit and electrodes to stimulate the common peroneal nerve and tibialis anterior to dorsiflex and slightly evert the foot. This technology has been used to improve the speed and symmetry of gait in patients with chronic hemiparesis [14]. The specific programming settings for this patient are provided in table 1. He was seen 3 times by the same physical therapist for training with the devices, and for functional measures of gait, training consisted of putting the devices on him and watching him walk at different settings over level terrain indoors, up and down stairs, ramps, and uneven terrain outdoors including grass, gravel, mulch, hills outside of building, paved parking lots and curbs. Training sessions were 90 minutes each. He was eventually able to successfully negotiate all terrains without physical assistance or use of a cane or walker. The same physical therapist performed outcome measure testing (gait velocity: 10 meter walk, 6 minute walk, functional gait assessment, and Timed Up & Go) both with and without the NESS L300 devices. These measures are well researched and have demonstrated reliability, validity and correlation to reducing falls risk. Specifically, the Functional Gait Assessment was selected as it assesses "dynamic balance". Other balance measures exist, such as the Berg Balance test. However the berg balance test measures more static balance and would not be expected to demonstrate a significant change in this setting.

| Setting | Right Side | Left Side |
|---|---|---|
| Intensity | 40 | 40 |
| Wave Form | Symmetric | Symmetric |
| Phase Duration (μs) | 200 | 200 |
| Pulse Rate (Hz) | 30 | 30 |
| Ramp Up Time (s) | 0.3 | 0.3 |
| Extended Percentage | 20 | 20 |
| Ramp Down Time (s) | 0.3 | 0.4 |

**Table 1:** Specific initial settings used on the NESS L300 devices attached to this patient's right and left legs.

## Results

With functional electrical stimulation, the patient improved in four separate outcome measures, and these data are provided in table 2. Gait velocity increased from 0.73 m/s without the devices to 1.0 m/s with the devices. This represents an improvement from "household" or "limited community" functional walking categories to a full "community" category [15]. For comparison purposes, the published normative gait speed for males aged 50-59 is 1.43 m/s [16].

| Measurement | Without FES | With FES |
|---|---|---|
| Gait Velocity (m/s) | 0.73 | 1.0 |
| 6-minute Walk (m) | 281.6 | 376.1 |
| Timed Up & Go (s) | 22.51 | 14.01 |
| Functional Gait Assessment Score | 10/30 | 22/30 |

**Table 2:** Functional outcomes with or without Functional Electrical Stimulation (FES).

The 6-minute walk test improved from 281.6 meters to 376.1 meters. Using the reference equations for this measure, we determined that this was an increase from 39.17% to 51.84% of his predicted distance [17].

Functional electrical stimulation reduced the length of the patient's "Timed Up & Go" (TUG) test, which has been well-studied and validated as a predictor of falls in older adults [18]. Adults with TUG times of greater than 13.5 seconds are considered at an increased risk of falls. The patient's times improved from 22.51 seconds to 14.01 seconds.

Finally, the Functional Gait Assessment (FGA) was used. This is a 10-item gait test of postural stability for which independent adults aged 50-59 score between 25-30 out of 30 points [19]. The patient's score improved from 10 to 22. Of note, scores ≤ 22 indicate an increased risk of falls in older community-dwelling adults [20].

Over 2 years of follow up by the same neurologist and physical therapist he has continued to do well. His gait assessments are unchanged. His NESS L300 settings have actually decreased over time. At his most recent visit, his intensity settings were reduced by 5 points bilaterally.

## Discussion

Functional neuroprostheses have the potential to benefit patients with a wide variety of neurologic ailments, and such a benefit has been shown in the case of a patient with PLS. While functional electrical stimulation devices such as the NESS L300 usually work by stimulating weakened muscles in order to achieve improved limb clearance, we postulate that the technology worked via a novel

mechanism. In this patient, it was the spasticity that provided excessive lower extremity stiffness during the swing and stance phases of gait. This led to reduced hip flexion, knee flexion and ankle dorsiflexion. The patient did not have dorsiflexion weakness per se, but was just unable to overcome the influence of the spasticity. We theorize that by reducing plantarflexion during swing phase of gait, the overall influence of the spasticity was reduced. This allowed the patient to flex his hip, knee and ankle more in swing with less stiffness rolling over his foot toward the terminal stance phase.

This patient clearly improved in all of the 4 functional outcome measures tested as compared to his own baseline established without the device. His results demonstrated improvement of function in a positive direction. This included a faster gait velocity, traversing a longer distance over the 6-minute walk test, reduced time on the Timed Up & Go (TUG), and higher score on the functional gait assessment. However, he remains below normal as compared to a healthy aged matched individual. The patient continues to have effects of spasticity secondary to PLS. However, compared to other traditional interventions including medication usage (including an implanted baclofen pump), standard bracing trials, use of assistive devices and spasticity management activities (stretches, reciprocal cycling patterns, use of warm water exercises), this patient had the most functional improvement through use of the NESS L300 FES devices. While the patient continues to be served by a multi-pronged approach to his disease management, the use of the neuroprostheses appears to have provided benefit in terms of function and mobility. We wondered how the progressive nature of PLS would affect his response to NESS L300 FES.

PLS is an uncommon disease and the technology is understandably in its nascence. As a testament to these two points, it is worth noting the difficult process of obtaining insurance approval for the devices at the devices' current cost. As it is well understood, the cost of new devices carry the expense of the research program and bringing the device to market. The process of successfully obtaining two devices for the patient created a significant challenge. A thorough letter of medical necessity was provided to outline the improvement in functional outcomes detailed in this report. In addition, the patient's neurologist advocated for the use of these devices not only by completing the required paperwork, but also by directly discussing the merits of this patient's case with the insurance provider's medical director. The patient also advocated for himself by working closely with the device manufacturer and his insurance carrier. While the result was successful, it still remains difficult to achieve provision and funding of bilateral neuroprostheses to all individuals with PLS.

In terms of alternatives to the NESS L300 FES, we have seen mixed results trying traditional bracing in patients with lower extremity spasticity including those with PLS. We have tried both flexible braces (posterior leaf spring braces) and more rigid ankle foot orthoses. The Posterior leaf spring braces are like traditional Ankle Foot Orthoses (AFOs) but thinner in the back. We have not found that articulated braces (or braces with a joint) have helped and they are heavier. In addition, braces with a dorsiflexion assist or loaded springs can increase spasticity. From a clinical observation, some patients with PLS appear to have improved limb clearance with traditional braces and exhibit an overall reduction in spasticity (as noted with improved hip flexion in the swing phase of gait). However, results across patients have been mixed. Often times, once we brace people with PLS, they require the use of a rollator walker to help compensate for the balance change. The rollator walker also helps with hip flexion in swing. Unfortunately most of our patients with PLS refuse to use these devices. They report feeling "locked up" and that their balance is worse. It makes sense that patients with increased stiffness in their limbs from the spasticity might feel this way with a rigid device. As a result, they fall frequently. Several have had serious injuries including fractures.

While this is a case study of one, we continue to selectively try this intervention with other patients affected with PLS and have seen other positive outcomes. There largest limitation of this case study is the lack of any documented norms across the age span in patients with this disease. Further research is needed to identify specific functional outcome measure norms and cut-off values for populations with PLS.

It is our goal that additional research will be conducted on the benefits of these technologies in patients with PLS in the hope that they may be more widely provided and covered for those who are suffering, particularly if such a sizeable benefit can be obtained. We also look to future studies that expand and improve upon the role of neuroprostheses for this and other neurologic disorders. If we are correct in the postulated mechanism of reducing the overflow of spasticity through the timely provision of electrical stimulation, patients with spasticity due to other diseases may also benefit.

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