THE ORTHOTIC AND THEREPUTIC EFFECTS OF PERONEAL NERVE FUNCTIONAL ELECTRICAL SIMULATION IN PARKINSON'S DISEASE: POST HOC ANALYSIS FROM A FEASIBILITY STUDY FOR A RANDOMISED CONTROL TRIAL

Taylor PN[1,2,3], Seary C[4], Sampson T[1], Beare B[4], Stevenson VL[4], Donavon-Hall M[5], Marques E[6], Padiachy D[1], Lee J[1],

[1]Salisbury NHS Foundation Trust, UK, [2]Odstock Medical Limited, UK, [3]University of Bournemouth, UK [4]National Hospital for Neurology and Neurosurgery, UK 5University of Southampton, UK, [6]University of Bristol, UK

p.taylor@salisburyfes.com

Abstract:

Design: A two-arm assessor blinded randomised controlled trial with an 18 weeks intervention period and 4 weeks post-intervention follow-up.

Participants: 64 participants with idiopathic Parkinson's Disease, reduced ankle movement and slow walking speed <1.25ms^{-1}.

Interventions: Functional Electrical Stimulation delivered to the common peroneal nerve while walking in addition to standard care compared with standard care alone.

Main measures: 10 metre walking speed, step length and Borg rate of perceived effort.

Results: The total orthotic effect for walking speed at week 18 was 0.12 ms^{-1} [CI 0.01, 0.23] and the therapeutic effect was 0.17 ms^{-1} [CI 0.06, 0.29]. For step length no meaningful total orthotic effect was found at week 18, 0.01 m [CI -0.04, 0.06]. However, a therapeutic effect was present, 0.05 m [CI 0.01, 0.09]. There was a small reduction in Borg score at setup -0.50 [CI -1.36, 0.36], which was not present at week 18.

Conclusion: The study design and intervention were feasible and suggestions are made for modifications to the protocol. Preliminary results suggest that while functional electrical stimulation can provide orthotic assistance, the therapeutic effect may be of more clinical significance..

Keywords: *Parkinson's Disease, Bradykinesia Functional Electrical Stimulation*

Introduction

Functional electrical stimulation has become a standard intervention for correction of dropped foot following upper motor neuron lesions in conditions such as stroke, multiple sclerosis and spinal cord injury[1]. In a series of observation studies, we have investigated the use of the technique with people who have Parkinson's Disease[2, 3]. Our initial hypothesis was that Functional electrical stimulation might be effective at overcoming freezing. However, the most prominent effect appeared to be a reduction in bradykinesia, demonstrated by increased walking speed after stimulation had been used. To determine clinical effectiveness of the technique we proposed a multicentre randomised control trial and in preparation for that trial, we performed a feasibility study. A paper reporting the main results of the feasibility study has been published[4]. That paper reported on the feasibility objectives and presented a summary of the data recorded by the assessors blinded to the participants group allocation. This paper reports data recorded by the treating clinicians and examines the immediate effect of using Functional electrical stimulation.

For people with a dropped foot due to stroke or multiple sclerosis, electrical stimulation devices are used as assistive devices, meaning that the principal benefit is received at the same time the device is being used. This has been demonstrated by increases in walking speed while using the device. When walking speeds are compared with and without the device on the same occasion this is referred to as an orthotic effect, or as a total orthotic effect if speed with the device is compared with unassisted walking at the beginning of treatment. It has also been noted that functional electrical stimulation may have a therapeutic effect, leading to an increase in walking speed when walking without the device, after the device has been used for a period. If the effect is short term, typically minutes to hours, it is referred to as a carryover effect and is thought to relate to increase excitability of the neurological system[5]. If the effect is longer in duration it is referred to as a training effect and may be due to additional effects such as muscle strengthening and motor relearning[6]. Typically, the orthotic effect is reported to be of more clinical importance than the therapeutic effect. In a case series of 111 people with dropped foot due to stroke who used a dropped foot stimulator for 18 weeks, a total orthotic effect of 0.16ms^{-1} [95%CI (Confidence Interval) 0.12, 0.20] and a therapeutic effect of 0.08ms^{-1} [95%CI 0.05, 0.11] were reported[7]. In a case series of 153 people with a dropped foot due to multiple sclerosis and used a dropped foot stimulator for 18 weeks, a total orthotic effect of 0.11 ms^{-1} [95%CI 0.08, 0.13] was reported[8] but no therapeutic effect was found, 0.00 ms^{-1} [CI -0.04, 0.03].

In this report we perform post hoc analysis, exploring the orthotic and therapeutic effects from the use of Functional Electrical Stimulation applied to the common peroneal

nerve of people who have Parkinson's Disease, while walking.

Method

For a full description of the study and participants please see our previous publication[4]. Briefly, the study was a feasibility randomised controlled trial and compared standard care with functional electrical stimulation used in addition to standard care. The treatment group used the intervention for 18 weeks and were followed up 4 weeks after the intervention was withdrawn. Participants had Parkinson's Disease with a Hoehn and Yahr Scale score between 1 and 4, a self-selected walking speeds of less than 1.25ms^{-1} and had reduced ankle movements while walking. Assessments were carried out in the "on phase" of Parkinson's, i.e. when medication was being effective.

Following the taking of consent, the baseline measures were recorded by an assessor blinded to the group allocation. The intervention group participants were taught how to use the device over two, one-hour clinic sessions separated by one week. The first session was either on the same day as randomisation, occurring after the blinded assessments or on a separate day, within one week of randomisation. The treatment group received the Odstock Dropped Foot Stimulator- ODFS®Pace, which was fitted to the leg the treating clinician identified as having the greatest deficit in dorsiflexion and eversion. Self-adhesive hydrogel electrodes (Pals #901220 50x50mm Axelgaard) were place over the common peroneal nerve at the head of fibula and over the motor point of the tibialis anterior. The current was set at a sufficient intensity to cause an active comfortable muscle contraction, correcting any deficit present in dorsiflexion and eversion. Stimulation parameters were typically; pulse width 180µs, frequency 40Hz, current 30-50mA. The participants were taught how to fit the device, how to identify the correct movement of the foot and how to adjust the position of the electrodes and intensity to produce this movement. The 10m waling test was recorded by the treating clinician at the second session and at six and eighteen weeks post randomisation. It was also recorded by the blinded assessor at six and eighteen weeks and additionally at 22 weeks.

The 10m walk test was recorded over a 12 m walkway, which included 1m at either end to account for acceleration and deceleration. Participants were given a single instruction, to "walk briskly but safely to the far line". The treating clinician recorded two walks without stimulation followed by one walk with stimulation and then one without stimulation in quick succession. The first is considered to be a warm up walk and is not included in the analysis. The second walk is representative of unassisted walking, the third with stimulation is used to determine the orthotic effect (walk 3-walk 2), while the fourth walk is used to determine the short-term carryover effect (walk 4-walk 2). The total orthotic effect compared the 10m walk test recorded by the blinded assessor at week 0 and the walking test with stimulation at week 18. For the therapeutic effect, the walking tests at 0 and 18 weeks recorded by the blinded assessor were compared. The number of steps taken between the 10m lines was used to calculate step length. At the end of each walk the participant was asked to estimate the effort used using the Borg rate of perceived effort scale (10 point version, lower number represents less effort)[9]. The blinded clinician used the same procedure but only

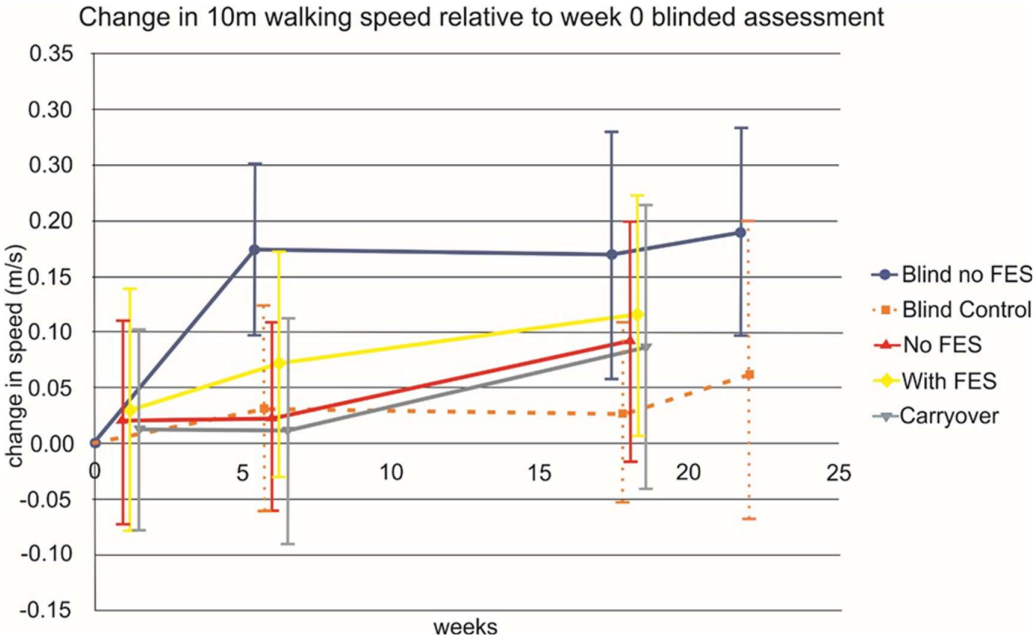

Figure 1. The change in walking speed relative to values recorded at week 0 by the blinded assessor. Mean with 95% confidence intervals. FES = Functional Electrical Stimulation.

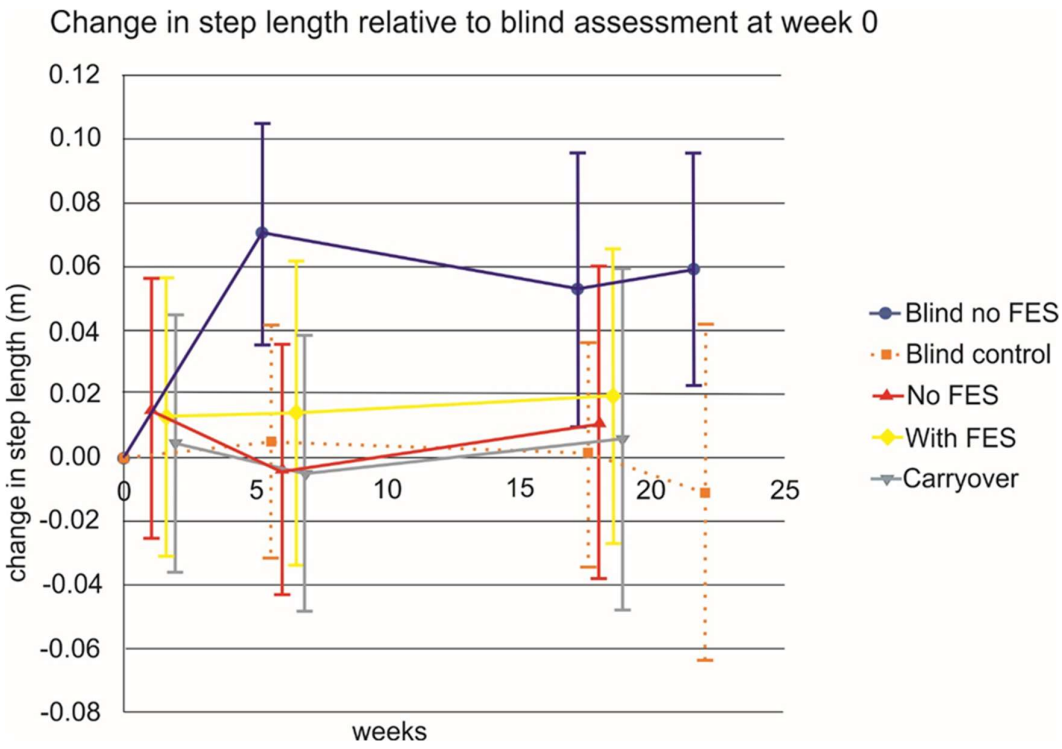

Figure 2. The change in step length relative to values recorded at week 0 by the blinded assessor. Mean with 95% confidence intervals. FES = Functional Electrical Stimulation.

recorded two walks, both without stimulation. The 2nd walk was reported. The Borg score was not recorded by the blinded assessor.

Results

Sixty-four participants were recruited, 32 to each group. The change in walking speed and step length relative to measures recorded by blinded assessor at week 0 are shown in figures 1 and 2.

The total orthotic affect for walking speed at week 18 was 0.12 ms^{-1} [95% CI 0.01, 0.23] (p=0.07) and the therapeutic effect was 0.17 ms^{-1} [95% CI 0.06, 0.28] (p=0.008) relative to the unassisted walking speed at week 0 measured by the blinded assessor. The therapeutic effect was maintained at week 22, 0.19 ms^{-1} [CI 0.10, 0.27] (p=0.0005). No short-term carryover effect was recorded at any point.

For step length no meaningful total orthotic affect at week 18 was found, 0.01 m [95% CI -0.04, 0.06] (p=0.13). However, a therapeutic effect was present, 0.05 m [95% CI 0.01, 0.09] (p=0.02) relative to the unassisted step length at week 0 measured by the blinded assessor. The therapeutic effect was maintained at week 22, 0.06 m [95% CI 0.02, 0.10] (p=0.003). Again, no short-term carryover effect was recorded at any point.

Fifteen participants reported that walking required less effort when stimulation was used at set up, while 8 reported that walking required more effort, giving an average change in Borg score of -0.50 [95% CI -1.36, 0.36] (p=0.19). At week 6 the number of participants reporting reduced effort with stimulation was 12 while 7 reported increased effort, resulting in no overall change in Borg score, 0.03 [95% CI -0.54, 0.60] (p=0.90). At week 18, 5 participants reported a reduction in effort, while 4 reported an increase and again there was no overall change in Borg score -0.04 [95% CI -0.44, 0.36] (p=0.84). No overall short term carryover effect was found at any time point.

Discussion

The results of this study add support to the hypothesis that functional electrical stimulation of the common peroneal nerve can reduce bradykinesia, demonstrated by increased walking speed after it has been used. Interestingly, although this was a small study and not powered for this analysis, in contrast to people with other neurological conditions, participants experienced a greater therapeutic effect than orthotic effect and no short-term carryover effect was observed. While participants reported a small benefit to the effort of walking at the start of the study, it appears that for the majority of participants the device had greater clinical utility as a training device rather than an assistive device.

Walking speed and step length were recorded while not using stimulation by both the treating clinician and the blinded assessor at each stage of the study. It is notable that different results were recorded, with the blinded assessors recording a larger increase in both parameters. At week 6 the difference in walking speed measure when not using FES between the assessors was 0.15 ms^{-1} [CI 0.04, 0.26] (p=0.018), a bigger difference than the minimum

clinically important difference[10] of 0.13 ms^{-1}. This was an unexpected result. The same procedure was used by all assessors. While at both study centres the blinded assessor and treating clinician measurements were performed in different rooms, both rooms were of similar size and laid out in a similar fashion. However, there were differences in procedure before the measurements were made. For the blinded session, participants were asked to attend the session not wearing the device. If they arrived at the clinic wearing the device, the receptionist would ask the participant to remove the device before entering the clinic room. The clinical assessments were performed in a set order with the 10m walking test being the first physical assessment, occurring after two questionnaires had been completed. In the treatment session, the participants were encouraged to attend wearing the device. The 10m walk test was performed towards the end of the session after the operation of the device had been checked, a process that would require the participant to walk several lengths of the gym while their walking was observed. There are therefore two principal differences. In the treatment session, the participants may have been more fatigued by walking further before the assessment, and that electrical stimulation had been used soon before the measurement had been made. This suggests that the stimulation may have had a short-term inhibitory effect, while in the longer term having an excitatory effect.

These observations lead to the following recommendations for the subsequent study. Firstly, participants should rest for a period of 10 minutes before completing the 10m walk test in the treatment session. Secondly, the time between stimulator use and the blinded assessments should be more tightly controlled by asking participants not to have used the device on the day of the assessments, before the assessment takes place. Finally, the possible short-term inhibitory effect may have implications for how functional electrical stimulation should be used, suggesting that a daily short period of use may be more effective than using the device whenever walking. Participants will therefore be asked to use the device for a short period daily and additionally at any other time if they feel it directly benefits their walking.

It was reported by some participants that intermittent use resulted in longer-term benefits, in some cases lasting several days[4]. This could be characterised as a carryover effect, as improvements occurred after a short period of using stimulation, which then declined before being renewed by another short period of stimulation. The therapeutic effect reported in this study may therefore perhaps be better described as a long-term carryover effect.

The observed differences in the benefits observed by participants of using functional electrical stimulation certainly warrants further elucidation and we hope these findings will guide future study design.

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