8 December 2017

FES USER DAY
The STEPS team

Paul Taylor PhD Chief Investigator and local PI, Consultant Biomedical Engineer, Head of Research, The National Clinical FES Centre, (study inception, design and management lead)

Ben Beare, Research Physiotherapist, STEPs study, UCLH
Trish Sampson, Research Physiotherapist, STEPs study, Salisbury

Co-Investigators
• Dr Diran Padiachy, Consultant Physician in General and Elderly Medicine, Salisbury NHS Foundation Trust (Medical lead)
• James Lee, Movement Disorder Nurse Specialist, Salisbury District Hospital (Recruitment lead)
• Sheila Nell, Chair of the Salisbury branch of the Parkinson’s Disease Society. (PPI lead)
• Paul Strike, Statistician, Research Design Service, Salisbury District Hospital (Study methodology)
• Maggie Donavon-Hall PhD, Health Psychologist, University of Southampton (Qualitative research lead)
• Elsa Marques PhD, Research Fellow in Health Economics, Bristol University (Health economics lead)
• Coralie Seary, Therapy Outpatients, The National Hospital for Neurology and Neurosurgery (Physiotherapy lead)
• Val Stevenson, The National Hospital for Neurology and Neurosurgery (Neurology lead and local PI)
• Peter Thomas PhD, Professor of Healthcare Statistics and Epidemiology, Bournemouth University (Statistical lead)

Patient Advisory Group
• Sheila Nell, Christopher Wadge, Gillian Wadge, David Houghton, Evelyn Houghton, Ronald Lines, Joyce Lines
AIM / Learning outcomes

What does STEPS stand for?
The PD patient - common issues for people with Parkinsons (pwPD)
  - 3 main PD symptoms
  - Common issues: PD/medication
  - Hoehn and Yahr Staging

Background to the STEPS study
Purpose of the STEPS study

Study Detail
  - Inclusion/Exclusion Criteria
  - Study Design
  - Outcome measures
  - Status

TIPS on FES use for pwPD from observations: Ax and Rx

Patient Funding Post Study
Case Study

Potential Mechanisms of FES in PD
What does STEPS stand for?

The Effectiveness of Peroneal Nerve Functional Electrical STimulation (FES) for the Reduction of Bradykinesia in Parkinson’s Disease:

A Pragmatic Two Site Feasibility Study for a Single Blinded Randomised Control Trial (STEPS).
3 main PD symptoms = parkinsonism

Tremor (shaking) - usually starts in the upper limb and is more likely to occur when the limb is relaxed and resting

Bradykinesia (slow physical movement) - results in a distinctive slow, shuffling walk with very small steps (festination).

Rigidity (muscle stiffness) – stiffness and tension in the muscles, making it difficult to move around and make facial expressions.
Common Problems in Parkinsonism and/or Side Effects of Medication

Lightheadedness
Insomnia/excessive daytime sleepiness
Vivid dreams/nightmares
Difficulty moving during sleep
Sadness/depression
Caregiver stress
Loss of motivation
Loss of pleasure from activities
Anxiety
Euphoria
Gambling
Dry or oily scalp or face
Dry eyes
Change in vision
Loss of sense of smell
Skin redness
Rash
Mole changes
Itching
Loss of facial expression
Swallowing problems
Weak voice
Tremor
Stooped posture
Nausea
Constipation
Diarrhea
Weight loss
Weight gain
Impotence/loss of orgasm
Decreased or increased sex drive
Loss of control of urine
Pain
Medication wears off suddenly
Extra squirming movements (dyskinesia)
Twisting postures (dystonia)
Hesitation/freezing
Problems walking
Swelling
Change in handwriting
Loss of dexterity
Change in sleep pattern

©2008 Movement Disorders Center • University at Buffalo Neurosurgery • 716-859-7580
Hoehn and Yahr Staging of PD

1. Symptoms on one side of the body only
2. Bilateral symptoms; no balance impairment
3. Impaired postural reflexes; physically independent
4. Severe disability, yet still able to walk or stand unassisted
5. Wheelchair bound or bedridden

Increasing Disability; Decreasing Independence

Hoehn and Yahr Staging
Background to the STEPS study

1. Mann et al. (2008)
   - 10 pwPD used FES for 2 months
   - Training effect – ↑ speed
   - ↓ FoG and Falls

2. Popa and Taylor (2013)
   - 11 pwPD (Hoehn and Yahr 2-3) used FES for 2 weeks
   - Training effect – mean ↑ step length and ↑ walking speed
   - ↑ health related QoL

3. Djurić-Jovičić et al. (2013)
   - 10 pwPD stimulated wrists, fingers and thumb for 30 min over 10 days.
   - Transcranial magnetic stimulation (TMS) showed ↑ cortical activity.
   - Also 21% increased hand mvt
Purpose of the STEPS study

pwPD often walk slowly and fall → a reduced quality of life
Small studies suggest patients walk faster and have reduced PD symptoms after using FES

STEPS is a feasibility, single blinded, multi-centre RCT to inform the design a larger RCT
- Recruitment rate, willingness to be randomised, loss to follow up
- Pt view on meaningful outcome measures
- Data to inform sample size calc, duration and cost of full RCT and to refine methods

FUTURE, larger RCT is to investigate whether:
- FES would be beneficial to patients in the longer term compared to routine care AND
- Value for money for the NHS.
Inclusion and Exclusion Criteria

**Inclusion criteria:**
Over 18 years

**Idiopathic Parkinson’s disease:** Hoehn and Yahr stages I to IV

**Gait difficulties:** reduced DF or eversion, bradykinesia $< 1.25\text{ms}^{-1}$, festination, akinesia (freezing), hypokinesia (short steps)

Can walk 10m with appropriate walking aids but without assistance from another person
Able to standing without the assistance of another person.
Medically stable defined as no significant changes in the participants condition over the last 3 months
Can give informed consent and can understand and comply with the treatment and assessment procedures

**Exclusion criteria:**
Faster than 8.0s over 10m (>12.5m/s)
Non standard drug therapy (DBS)
Atypical or secondary parkinsonism or parkinsonism related to other neuro degenerative diseases, pyramidal and/or extrapyramidal systems injuries
Untreated or refractory epilepsy (fits in last 3 months), pregnancy, cardiac pacemaker, or other active medical implanted devices, malignancy or dermatological conditions in the area of the electrodes
Denervation of the common peroneal nerve or other neurological condition known to cause dropped foot
Severe osteoarticular pathology that significantly affects walking
Major cognitive impairment; dementia.
Study Design

Group 1: Control

Group 2: FES

Group 2: NO FES

Timeline:
- Week 0
- Week 6
- Week 18
- Week 22

Treatment and non-blinded assessment schedule

Group 2 only:
- 2 sessions to set up and teach device use and non-blinded assessments
- 1 follow up session to ensure continued effective device use and non-blinded assessments
- Final non-blinded assessments & return of FES equipment to clinic

Normal FES treatment procedure

Blinded assessment schedule

Groups 1 & 2:
- Week 0: Recruitment, consents, screening and baseline assessments followed by randomisation (PI)
- 6 week: Interim assessments
- 18 week: End of intervention assessments
- 22 week: Training effect assessments

Additional for the study:
- Falls and health resource use diary throughout the study week 0 to 22

Telephone interviews Groups 1 & 2

Prior to intervention to explore aspects of walking that are important to pwPD & Reasons for not taking part if participation is declined

Participants who drop out from the study as they drop out

At the end to find out what participants thought of FES and of taking part in the study

Additional for the study
STEPS Outcome Measures

Semi-structured interviews
PDQ-39 (QoL questionnaire)
10mWT (+ number of complete steps)
UPDRS part 1-4 (impairment, activity and participation - 50Q)
A/PROM and MRC
N-FOG (freezing)
FES-I (fear of falling)
Health resource use (Bristol)
MiniBEST (which includes TUG)
EQ-5D-5L
Falls Diary
Status of the study

End March 2018 all participants finish

<table>
<thead>
<tr>
<th>Centre</th>
<th>Recruited</th>
<th>Completed</th>
<th>Withdrawn</th>
<th>Still in trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salisbury</td>
<td>33</td>
<td>25</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>London</td>
<td>31</td>
<td>18</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Totals</td>
<td>64</td>
<td>43</td>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>

Analysis

Write-up
Observation of pwPD gait

- Reduced arm swing and step length
- Unilateral or bilateral foot drop / scuffing
- ‘slow shuffling gait’ / festination
- Difficult to initiate walking, may stop abruptly or can’t stop!
- Turning - difficult and slow
- Freezing
- Bradykinesia but can also have slow mental processing
- TUG > 11.5secs can predict falls in pwPD (Nocera et al, 2013)
TIPS on FES use for pwPD

Default settings for PD:
  R-Ramp=150, Ext=150, F-Ramp=50
  SYM waveform
  Pulse width to start on 50%
  TA stimulation

TUG and 10mwt as outcome measures

Observation:
  Potentially training effect > orthotic effect
  Queueing effect - consider leaving sounder on?
Patient Funding Post Study

11 pwPD from STEPS (Salisbury) are using FES. 9 pwPD have secured funding - Wiltshire & Hampshire including 2 from the control group.

A couple of pwPD pay privately (Dorset, Northampton)

Process for Funding:
Letter to GP giving rationale for funding:
  description of gait,
  if in FES group how they responded, and compliance in the trial
GP referral to OML
OML raises IFR request to CCG
TRAINING EFFECT - FES group (1056)

**Dx:** 11 years PD,

**Hx:** Tripping – #hand, tremor L foot, restless legs, breast Ca, migraine, no freezing

**PD Meds:** Amantadine, rasagiline, sastravi, co-careldopa and pramapexole

**GAIT:** scuffing L foot, ↓ arm swing and fwd stooped

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>0 wks</th>
<th>6 wks</th>
<th>18 wks</th>
<th>22 wks</th>
<th>Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>10mwT (sec)</td>
<td>9.8</td>
<td>8.1</td>
<td>7.4</td>
<td>7.4</td>
<td>-24%</td>
</tr>
<tr>
<td>Steps</td>
<td>21</td>
<td>16</td>
<td>15</td>
<td>15</td>
<td>-29%</td>
</tr>
<tr>
<td>TUG (sec)</td>
<td>14.7</td>
<td>12.1</td>
<td>12.5</td>
<td>14.8</td>
<td>-15%</td>
</tr>
<tr>
<td>TUG dual (sec)</td>
<td>25.1</td>
<td>15.6</td>
<td>18.2</td>
<td>18.4</td>
<td>-27%</td>
</tr>
<tr>
<td>Minibest (/28)</td>
<td>12</td>
<td>17</td>
<td>16</td>
<td>16</td>
<td>33%</td>
</tr>
</tbody>
</table>

**Comments** “feels better with it”, “does not have to think about foot!”

Wiltshire funded!
ORTHOTIC EFFECT- Control group (1068)

Dx: 4 yrs PD, T2DM, Stent >10yrs
PMH: Walking deteriorated, L hand tremor, falling, stumbling, freezing >1yr
PD Meds: Madopar and others ++

GAIT: lateral lean L, turning difficult, festination, freezing
GAIT FES: larger steps, no freezing (doorways, enclosed cubicle)

<table>
<thead>
<tr>
<th>10mwt</th>
<th>Time (secs)</th>
<th>Speed (m/s)</th>
<th>Borg RPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>No stimulation 2</td>
<td>14.0 (24)</td>
<td>0.71</td>
<td>5</td>
</tr>
<tr>
<td>With FES</td>
<td>10.4 (18)</td>
<td>0.96</td>
<td>2</td>
</tr>
<tr>
<td>Orthotic effect</td>
<td></td>
<td>35%</td>
<td>-3</td>
</tr>
</tbody>
</table>

Comments “feels cueing effect from FES”, “reduced my freezing”, “more confident and less FoF”

Northampton funded!
Potential Mechanisms of FES in PD

Providing **sensory external cue**

**Biomechanical** – providing muscle contraction of weakened dorsiflexors/evertors (weak potential due to reduced central initiation stimulus)

Potentially causing **cortical excitation effects** - only small no. TMS studies indicate this.

Antidromic firing of peripheral nerve resulting in **excitation of the anterior horn cells**, reducing motor nerve stimulation thresholds = training effect
DISCLAIMER:
This presentation presents independent research funded by the NIHR under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-1014-35012).

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Mann GE, Finn SM, Taylor PN. A pilot study to investigate the feasibility of electrical stimulation to assist gait in Parkinson’s disease. Neuromodulation 2008; 11(2): 143-149.


This study found an immediate reduction in episodes of freezing when FES was used.