FIBROMYALGIA TENS IN PHYSICAL THERAPY STUDY (FM TIPS)

KICK OFF MEETING – NOVEMBER 19, 2019
PARTNERSHIP BETWEEN THE COLLEGE OF PUBLIC HEALTH AND THE CARVER COLLEGE OF MEDICINE AT THE UNIVERSITY OF IOWA AND VANDERBILT UNIVERSITY
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  • Richard Peters
  • Trevis Huff
  • Andrew Post
  • Carol Vance
  • Bridget Zimmerman

• Design and Analysis Team
  (Bayman and Zimmerman)
  • Janel Fedler
  • Jon Yankey
FIBROMYALGIA IS ASSOCIATED WITH WIDESPREAD PAIN, CO-MORBID SYMPTOMS, AND CENTRAL SENSITIVITY

Fibromyalgia Diagnostic Criteria 2016²

1. Generalized pain
2. >3 months
3. Fibromyalgia Severity
   a. Widespread pain index
   b. symptom severity scale score

¹Mansfield 2016, ²Wolfe 2016
TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

- Application of electrical stimulation to the skin for pain control (APTA 1990)

**Outcome Measures**
- Pain
- Hyperalgesia
- Function

**Frequency**
- <10 Hz = low
- 50-100 Hz = high

**Intensity**
- Sensory
- Motor

**Electrode Placement**
- Site of Injury
- Dermatone
- Nerve Root

**Pulse Duration**
- 10-250 µs
TENS USES ENDOGENOUS INHIBITORY MECHANISMS TO PRODUCE ANALGESIA

Low Frequency TENS

From PAG

- Opioid
- Nociceptive neuron (ON cells)
- Decreased activity

To Spinal Cord

- Serotonergic neuron
- Increased activity

Decreased sensitization

- From RVM serotonin
- Nociceptive neuron

High Frequency TENS

- Opioid
- GABA
- Nociceptive neuron

- Decreased sensitization
- Decreased glutamate release

- From RVM

- From PAG
PATH TO FM TIPS:

Animal Model
1998 High or Low Frequency TENS

Translational Model
2012 Knee OA

Clinical Model
2013 TENS 1x Treatment with FM

Clinical Model: FAST
2013-2018 Fibromyalgia Activity Study with TENS

FM TIPS 2019
TENS DOSING IS CRITICAL TO EFFECTIVENESS

Clinical Message

1. Intensity set as “strong but comfortable”
2. Give instructions to increase as able
TENS REDUCES MOVEMENT AND RESTING PAIN

Mixed Frequency

Active-TENS, n=103
Placebo-TENS, n=99
No-TENS, n=99

Dailey et al., 2019
TENS IMPROVES GLOBAL RATING OF CHANGE

NNT=3

To decrease movement pain

Dailey et al., 2019
# Responder Analysis

## Responder Definitions

<table>
<thead>
<tr>
<th>Responder Definition</th>
<th>% Responder (95% CI)</th>
<th>Risk Difference (adjusted 95% CI)</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active-TENS</td>
<td>44% (34, 53)</td>
<td>22% (15, 31)</td>
<td>0.004</td>
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<tr>
<td>Placebo-TENS</td>
<td>22% (15, 31)</td>
<td>14% (9, 22)</td>
<td>&lt;0.001</td>
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<td>No-TENS</td>
<td>14% (9, 22)</td>
<td>22 (6, 37)</td>
<td>30 (15, 44)</td>
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<tr>
<td>Active-TENS vs Placebo-TENS</td>
<td>22 (6, 37)</td>
<td>0.004</td>
<td>&lt;0.001</td>
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<tr>
<td>Active-TENS vs No-TENS</td>
<td>16 (3, 29)</td>
<td>0.018</td>
<td>16 (3, 29)</td>
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<tr>
<td>≥20% reduction in fatigue</td>
<td>45% (35, 54)</td>
<td>26% (19, 36)</td>
<td>0.019</td>
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<tr>
<td>≥20% improved function</td>
<td>36% (28, 46)</td>
<td>28% (20, 38)</td>
<td>10 (-6, 25)</td>
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<tr>
<td>≥30% reduction in pain and ≥20% reduction in fatigue</td>
<td>29% (21-39)</td>
<td>13% (8, 21)</td>
<td>0.018</td>
</tr>
<tr>
<td>Dailey et al., 2019</td>
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</table>
FIBROMYALGIA TENS IN PHYSICAL THERAPY STUDY (FM TIPS)
STUDY OVERVIEW

▪ **Goal:**
  ▪ Demonstrate the feasibility of adding TENS to treatment of patients with FM in a real-world Physical Therapy practice setting and
  ▪ Determine if addition of TENS to standard Physical Therapy for FM reduces pain, increases adherence to PT and allows patients with FM to reach their specific functional goals with less drug use.

▪ **Hypothesis**
  ▪ Using TENS in a Physical Therapy setting is feasible and that FM patients using TENS are more likely to reach their therapeutic goals.
UG3 AIM 1: PLANNING YEAR

RECRUIT PHYSICAL THERAPY PRACTICES AS RESEARCH SITES FOR AN EMBEDDED PRAGMATIC CLINICAL TRIAL, UNDERSTAND USUAL PT PRACTICE FOR PATIENTS WITH FM TO INFORM TRIAL PROCESSES, AND DEVELOP IMPLEMENTATION PROCEDURES

- Recruit community PT clinics willing to offer TENS as an adjunct to usual care for FM
- Perform interviews with front-line providers to evaluate PT-interventions for FM
- Evaluate potential barriers to TENS use during routine PT practice
UG3 AIM 2: PLANNING YEAR

ENSURE ADEQUACY OF INFRASTRUCTURE AT POTENTIAL STUDY SITES TO COMPLETE A PT EMBEDDED PRAGMATIC TRIAL

- address regulatory issues
- develop data extraction methods from EHR
- develop electronic consent forms
- develop electronic case report forms
- develop a manual of operating procedures
- pilot test to refine materials and procedures
UH3 AIM 1: DETERMINE IF ADDITION OF TENS TO ROUTINE PT IMPROVES MOVEMENT-EVOKED PAIN

UH3 AIM 2: DETERMINE IF ADDITION OF TENS TO ROUTINE PT IMPROVES 1) DISEASE ACTIVITY, 2) LIKELIHOOD OF MEETING PATIENT-SPECIFIC FUNCTIONAL GOALS, 3) ADHERENCE TO PT, AND 4) MEDICATION USE

UH3 AIM 3: EXAMINE FEASIBILITY OF IMPLEMENTING TENS INTO ROUTINE PT CARE FOR FM USING SEMI-STRUCTURED EXIT INTERVIEWS OF PATIENTS AND PTS

Cluster-randomized pragmatic trial

Routine PT with or without TENS for FM

Enroll ~600 people with FM
MILESTONE: SELECTION OF CLINICS (=20 CLINICS)

**Kepros Physical Therapy and Performance** – Iowa, local
Carla Franck, a PT with Kepros Physical Therapy will be part of the study team to help develop outcomes and training procedures for implementation of the trial

**Genesis Healthcare Systems** - Quad Cities, Iowa and Illinois
15 outpatient PT practices which see 200-300 FM patients per year

**Vanderbilt University Physical Therapy Services** - Nashville, TN
2 clinics that see approximately 100 people with FM per year

**BenchMark Physical Therapy**- Tennessee and Kentucky
regional network identified (approximately 10-15 sites)

**Rock Valley Physical Therapy** – Iowa and Illinois
>50 sites in rural and city environments

**Results Physical Therapy** – Tennessee
>50 sites rural and city environments
MILESTONE: DRAFT PROTOCOL

Participants

- **Inclusion:**
  - Individuals referred for land-based PT who have been diagnosed by a physician with FM
  - Primary diagnosis prompting referral or referred for axial pain

- **Exclusion**
  - Unwilling to use TENS
  - TENS contraindications

- **NOTE:** FM Diagnosis will be confirmed using instruments filled out by participants
Randomize by PT clinic site – TENS vs. no-TENS

TENS applied during activity – in clinic and at home

Data collected at PT clinic visits electronically and over phone
STUDY DESIGN

- Consent and initial evaluation
- Standard PT Treatments with or without TENS
- 2-3 month PT Follow-up Primary Outcome
- 6-month Follow-up
**Pain.** Pain during activity (movement-pain, primary outcome), and at rest (secondary outcome) using a 0-10 NRS

**Patient-Specific Functional Scale (PSFS)** - patient identifies 2-5 functional goals for the treatment plan, and rates their ability to do these on an 11-point scale: 0 unable to perform activity and 10 able to perform at the same level as before problem

**Patient-Reported, Validated**

Fibromyalgia Impact Questionnaire (FIQR), 21-item disease specific questionnaire that is divided into 3 domains: function, overall impact, and symptoms.

- The FM 2016 diagnostic criteria is a simple assessment that the patient can self-report and allows for determination of a Widespread Pain Index, Symptom Severity Scale, and Fibromyalgia Severity Score.
- PROMIS modules

**HEAL common dataset** - BPI, MOS-Sleep, PCS, Depression PHQ-2, Anxiety GAD-2, PGIC, TAPS.

**Patient Adherence Indicators.** EHR queries of data recorded at follow-up visits: Record if the patient used TENS, attended PT, or performed their home exercise program.

**Medications** collected through the EHR and patient report. We will ask both FM medication and doses, and prn medications and usage (opioids, NSAIDs, Tylenol).

**Additional questions for patients** at the follow-up visit will include ease of TENS use, barriers to TENS use, and general perceptions about TENS for pain control

**Exit interview questions of all PT providers** about use of TENS in PT practice for FM and chronic pain to assess likelihood of continued use, provider perceptions on usefulness of TENS for patients, barriers to TENS use in the clinic, perceived barriers to TENS use by patients

**MILESTONE: OUTCOMES**

- **JAN 2020**
  - Selection of Clinics

- **MAR 2020**
  - Central IRB
  - Protocol to NIAMS

- **May 2020**
  - Reliance Agreement 2 sites

- **JUNE 2020**
  - Training Materials

- **SEPT 2020**
  - Reliance Agreements All Sites
<table>
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<tr>
<th>Executive</th>
<th>Regulatory &amp; Protocol Development</th>
<th>TENS</th>
<th>Logistics</th>
<th>PRO/Data Collection</th>
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<tr>
<td>Sluka*</td>
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<td>Zimmerman</td>
<td>Ecklund</td>
<td># Ad Hoc: Dailey, Franck</td>
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</table>

**Monthly/Bi-Monthly**
- Weekly
- Weekly
- Weekly
- Weekly
- Weekly

**Tasks to achieve Milestones**

- **Oversee operations**
  - MOP
  - Evaluate TENS unit
  - Instrument Administration
  - Instrument selection
  - Clinic Interviews

- **NIAMS Protocol**
  - Test units in people
  - Contacting sites
  - Data management
  - Site Selection

- **Operational Training Materials**
  - Evaluate cost of units
  - MOP development
  - Statistical analysis Plan
  - Recruitment Strategy

- **CIRB**
  - Develop education and training materials for TENS
  - Training materials
  - Power analysis
  - Site Training- CITI and protocol

- **Site selection and contracts**
  - Protocol for ordering and tracking TENS units
  - Pilot Test Protocol in Clinics
  - Interviews with selected PT's
  - Recruitment
<table>
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<tr>
<th>Barrier</th>
<th>Level of Difficulty*</th>
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<tr>
<td>Enrollment and engagement of patients/subjects</td>
<td>x</td>
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<tr>
<td>Engagement of clinicians and health systems</td>
<td>x</td>
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<tr>
<td>Data collection and merging datasets</td>
<td>x</td>
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<tr>
<td>Regulatory issues (IRBs and consent)</td>
<td>x</td>
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<tr>
<td>Stability of control intervention</td>
<td>x</td>
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<tr>
<td>Implementing/delivering intervention across healthcare organizations</td>
<td>x</td>
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</table>

1=easy, 5=difficult
DATA SHARING UG3

- What is your current data sharing plan and do you foresee any obstacles?
  - Publish data in peer-reviewed journal
  - Post final data set on central server at University of Iowa

- What information did the IRB require about how the data would be shared beyond the study in order to waive informed consent, if applicable?
  - We are not waiving informed consent

- What data you are planning to share from your project (individual-level data, group-level data, specific variables/outcomes, etc.)?
  - Individual Level Data