Neubie for Low Back Pain Protocol
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Protocol Title
Efficacy of Pulsed Direct Current Electrical Stimulation (Neubie) on Low Back Pain

Abstract
This study will compare two methods of electrical stimulation (alternating current and direct current) as an adjunctive therapy to treating lumbosacral radiculopathy. Both types of electrical stimulation have been used in clinical practice for physical therapy, however direct current stimulation is much less common and there is less known about its impact on physical therapy outcomes. The aim of this project is to show the efficacy of a novel device, the Neubie direct current device, compared to traditional TENS unit in clinical physical therapy treatment of radiculopathy. Outcomes measured will include: pain intensity, functional status, and patient satisfaction.

Investigators
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Research Purpose and Hypothesis

Chronic low back pain (CLBP) affects a significant portion of the global population, with estimates suggesting that approximately 10-20% of adults experience chronic pain lasting for more than three months[1]. The condition can lead to significant disability, impaired quality of life, and substantial healthcare costs. Traditionally, non-surgical treatment for back pain has focused mainly on physical therapy combined with steroid injections or non-steroidal anti-inflammatory drugs, which are temporary solutions and are associated with multiple side effects including pain at the injection site, fever, and occasionally infection[2–4]. With this large patient population, there is a great need for non-invasive physical treatments that can avoid long-term pharmacologic dependence or injections. Technological advancements in physical therapy treatments can assist in meeting this need. One non-invasive physical therapy tool for back pain that has shown promise is the use of electrical stimulation (e-stim), a therapeutic modality where muscles and nerves are stimulated with electrical current via surface electrodes to stimulate muscular activation to improve strength and range of motion[5]. This

method has been widely used for the management of nonacute low back pain[6], and it is plausible that this method has greater potential to address other symptoms associated with low back pain such as muscle tension and weakness. E-stim has no long-term side effects, no known drug interactions, and has been shown to shorten treatment times, improve quality of life, and help reduce therapy costs by alleviating pain, inflammation, and muscle tension[7–10]. Transcutaenous e-stim is performed through the use of a device that sends gentle electrical pulses through the skin into muscles, joints, bones, and nerves.

The literature on the use of e-stim for treating back pain symptoms demonstrates the capability of the modality to alter chronic pain. Cutaneous circulation is significantly increased with the application of e-stim[11,12], but in addition, there is evidence of increased vascular endothelial growth factor (a primary angiogenic factor)[13,14]. This increase suggests that e-stim may increase angiogenesis, which in turn may improve microcirculation, leading to reduced symptoms and improved nerve function overall[13,14]. Further, the application of e-stim stimulates cutaneous afferent fibers, which may contribute to reported analgesic effects[12]. Pre-clinical studies suggest that e-stim inhibits nociception at the presynaptic level in the dorsal horn, effectively reducing pain by limiting the transmission of pain signals[15]. E-stim has been found to be efficacious for postoperative pain and pain after trauma[10,16,17].

There are a number of clinical studies that have investigated the use of e-stim for back pain[6,18,19]; however, generally these studies do not have control groups and were lacked objective measurements with results based solely on subjective questionnaires and pain assessment scales. Other clinical studies using e-stim for neuropathy, a common comorbidity of back pain, have found that direct current (DC) neuromuscular e-stim at higher frequencies is significantly more effective than alternating current (AC) e-stim like TENS at ameliorating symptoms such as reduced motor function and numbness[20–23].

This difference in efficacy between high frequency e-stim and TENS may be in part due to the use of higher frequency DC as opposed to AC. The unidirectional flow of DC fields is more useful for rehabilitation work as it is achieves greater input to sensory afferent signaling compared to the bidirectional flow of AC, which can cause a co-contraction that suggests both input and output stimulation of the nervous system. In contrast, DC allows for more specific contractile movement at higher amplitudes, making it more useful and efficient for training and rehabilitation[24]. Further, activation of denervated muscles requires a longer pulse length, achievable with DC but not with AC[25]. Importantly, one study showed that using DC e-stim for low back pain penetrated deeper into the tissues and resulted in a significant decrease in pain and improvement in function in patients suffering from low back pain on both subjective and objective outcomes, and was more effective and efficient than TENS[5].

The current evidence suggests that DC e-stim may be an effective therapeutic avenue for improvement and management of back pain. Historically, however, DC current has been less useful in the clinical setting, as the continuous unidirectional flow of ions leads to a buildup of charge that can cause skin irritation. The Neubie DC Electrical Stimulation Device offered by Neurological Fitness Equipment and Education LLC (NeuFit) is a neuromuscular electrical stimulation device that uses DC e-stim to stimulate muscle activation, blood flow, and the nervous system. The Neubie device uses a DC frequency via conductive pads placed at the targeted areas and counters the issue of irritation with an additional waveform that eliminates

skin irritation by dissipating heat and any charge buildup caused by the DC stimulation. The Neubie device is FDA cleared for the following indications: 1) Maintaining or increasing range of motion, 2) Increasing local blood circulation, 3) Neuromuscular re-education, 4) Preventing atrophy, 5) Reducing spasms, 6) Preventing venous thrombosis after surgery, 7) Management or relief of chronic pain, and 8) Management of post-surgical and post-traumatic acute pain. The only two contraindications are: 1) the presence of a cardiac pacemaker and 2) pregnancy. In validation of the Neubie's unique impact, a recently published study has demonstrated that treatment of neuropathy with the Neubie device resulted in statistically significant improvements in pain, vibration sense, and two-point discrimination, as well as improving nerve conduction velocity, distal latency, and amplitude, as measured by electromyography (EMG), and as compared to treatment with TENS, which showed no significant improvements in any outcome measures[26]. These findings further support the uniquely suitable use of the Neubie in treatment of low back pain, as it can improve range of motion, increase local blood circulation, prevent atrophy, promote neuromuscular re-education, reduce spasms, and decrease chronic pain.

The aim of the current study is to assess the effects of treating low back pain using DC e-stim delivered by the Neubie. The study assesses the efficacy of the Neubie on reduction of pain, improvement in range of motion of the lumbar spine, and improvement in mobility. We hypothesize that combined therapy including exercises and use of DC e-stim over a 4-6 week course of twice weekly physcial therapy will result in greater and/or more rapid improvement in all outcome measures (Modified Owestry Pain Scale, Visual Analog Pain Scale, Schober test for mobility and Quality of Life Index). These measures provide both quantitative and qualitative data on the severity of back pain symptoms.The results of this study could impact future recovery protocols not just for back pain, but for other conditions that result in nerve damage, muscle weakness, and chronic pain.

Research Design and Methodology

Subjects:

Patients over the age of 17 presenting to EA Therapeutic Health physcial therapy practice in Rochester MN with axial low back pain will be offered study inclusion if they meet inclusion and exclusion criteria. Eligible subjects will sign informed consent, and will be enrolled in a 4 to 6 week treatment regimen at EA Therapeutic Health.

Subjects will be assigned to either the control group (standard of care) or the experimental group (Neubie) through a randomization process: All subjects will be assigned a number after completing screeningand informed consent. A block randomization method will be created using the Graphpad randomization calculator web application (https://www.graphpad.com/quickcalcs/index.cfm) to build two groups of equal size (control and experimental), with a block size of 4.

Methods:

To determine the efficacy of direct current electrical stimulation (the Neubie device) on back pain, patients presenting with mechanical, non-radicular low back pain will enroll in a 4 to 6

week treatment regimen at EA Therapeutic Health. The first session will consist of an intake evaluation session that will include: Modified Owestry Pain Scale, The Schober test for mobility, Heart Rate Variability, and Quality of Life Index. These tests will serve as baseline (and a within subject control) for the intervention.

Participants will then undergo a treatment protocol that incorporates either traditional PT exercises (standard of care control) or PT exercises with the Neubie utilized concurrently (experimental group). Subjects will undergo an evaluation session prior to starting treatment that includes the Modified Owestry Pain Scale, The Schober test for mobility, Heart Rate Variability, and Quality of Life Index.

The experimental group subjects will undergo 12 sessions of physical therapy over a 4 to 6-week period which include 45 min of various physical therapy exercises concurrently with the Neubie followed by a 15 minute passive Vagus nerve stimulation protocol with the Neubie.

Control group subjects will participate in a physical therapy protocol that includes manual therapy (e.g. trigger point release, mobilization of the SI joint) and exercises for back strengthening and stretching. Experimental group subjects will participate in a physical therapy protocol that includes manual therapy (e.g. trigger point release, mobilization of the SI joint) and exercises for back strengthening and stretching in conjunction with Neubie DC e-stim. Both control and experimental groups will receive a customized Home Exercise Program with exercises to be performed at home 1 time a day.

Sample size: A power analysis was performed to determine appropriate minimum sample size for recruitment. Based on a power analysis using G*Power, we will analyze our data using a repeated measures ANOVA for within-subject factors (baseline vs post treatment). A sample size of 42 subjects, 21 in each arm, is sufficient to detect a clinically meaningful difference of 0.5 between groups assuming an effect size of 0.8 between means with 80% power and a 5% level of significance. Considering a dropout rate of 10%, the sample size required is 46 (23 per group).

Data Collection Methods

Data will be collected via objective/observational measurements taken by staff trained at EA Therapeutic Health. Consent forms and data will be stored in a HIPAA compliant EMR system and a locked cabinet. Data will be kept for a period of 5 years after the final report has been produced. Thereafter, the data will be destroyed. Detailed description of these measurements is included in the methodology section. Data analysis and manuscript preparation based on findings will be performed by Melanie Brennan, PT, DPT (co-PI) and Ramona von Leden, PhD (Vice President of Research and Clinical Affairs at NeuFit).

Participant data will be analyzed to test for an intervention main effect and symptoms at beginning and end of treatment completion (time X intervention). Measurements at the final treatment session will be compared to baseline with an ANOVA (significant changes– baseline vs session #) as a within-subject factor.

Tools for Data Collection

Time commitment for participants: 12 hours over 4-6 weeks (1-hour sessions, frequency detailed below).

Materials Needed:

NEUBIE device

Electrodes

Carbon Fiber Pads

Intervention/Treatment Protocol

Duration and Number of Treatment Sessions: Participants will undergo 12 treatment sessions over the course of 4-6 weeks. Treatments will be roughly 60 minutes per session – 45 minutes of physical therapy exercises (either standard of care OR DC e-stim as outlined below + 15 minutes Vagus nerve stimulation via the "master reset" program). Additional time will be needed for the initial evaluation session and the 12th or final session for clinical measurements/outcome measures. Outcome measures will be collected at baseline (initial evaluation session) and after the 12th or final treatment session.

Stimulation with the Neubie (Experimental Group)

Standardized stimulation frequencies: Electrical frequencies used are standardized via NeuFit's protocols. The pulses per second (PPS) determine the type of stimulation being provided. Frequencies on the Neubie range from 1-500 PPS. The PPS designated here (500 PPS) causes a smoother stimulation (rather than intermittent contractions) that results in relaxation to support increased range of motion, strength and stimulation of blood flow.

Electrical stimulation pad placement and intensity: Neurostimulation pads (either rectangular or circular) are linked to electrodes (designated red and black) for paired placement on the skin. Pad colors determine polarity of electrical current (Red = positive, Black = negative; typical direction of electron current flow is Black to Red).

For the PT exercises component of treatment, pad placement will be on the back and hips, with specific location determined by the physical therapist. Participants will be asked to perform exercises actively while receiving stimulation with the Neubie at their "treatment threshold". Treatment threshold will be described as "productively uncomfortable," but not "painful" (a 7 out of 10 on a perceived intensity scale). While being stimulated, participants will be asked to undergo a variety of PT exercises to mobilize their back and hips.

For the Vagus nerve stimulation portion of treatment, pad placement is standardized by the Neubie "Master Reset" protocol: red circular pads will be placed bilaterally at the upper cervical spine under the mastoid process, and the black pads will be placed bilaterally on the balls of the feet. Participants will be asked to lie passively for 15 minutes while receiving stimulation with the Neubie at a "comfortable" intensity (a 4 out of 10 on a perceived intensity scale). This protocol is believed to increase parasympathetic activity of the autonomic nervous system via external stimulation of the vagus nerve and support relaxation and recovery after

exercise therapy.

Standard of Care (Control Group)

Participants designated to the standard of care group will receive 45-60 minutes of physical therapist supervised exercises.

Outcome Measures

Pre and post treatment paradigm (at baseline and after 12th or final session) - the following variables will be evaluated: Modified Owestry Disability Index, Visual Analog Pain Scale, The Schober test for mobility and Quality of Life Index.

Procedures and Risks

Risks associated with participation in this study are minimal and no greater than those experienced during a routine physical therapy intervention. DC e-stim has been employed in physical therapy practice for over 40 years. Risks associated with electrical stimulation include mild discomfort caused by the sensation of the electrical stimulation (buzzing, tingling), and possible delayed onset muscle soreness (DOMS) after sessions.

This therapy is non-invasive, and stimulation intensity is governed by the participant. The patient will be asked to tolerate some discomfort with a perceived intensity level of 7 out of 10 but will never be asked to tolerate intensity that causes pain. Further, they will be monitored for the duration of the sessions by their practitioner and will never be left alone while being treated with DC e-stim.

Potential Benefits

It is expected that both control and experimental groups will have improvement in their axial low back pain over the course of physical therapy.Such improvements in pain could significantly benefit participants' quality of life, sleep quality and physical function, and allow quicker return to work.

Benefit to Society The use of a non-invasive medical device like the Neubie for treatment of back pain could have several major benefits. Most substantially, it could validate a treatment that could be used in both a clinic setting, or with proper training, at home by patients, to mitigate back pain and keep it from worsening or reoccurring. It could also help in understanding the use of electrical stimulation in rehabilitation for acute and chronic pain conditions, and neuromuscular re-education.

Data Safety Monitoring

The study does not have a data and safety monitoring board, but the researchers have an internal plan for data and safety monitoring. Safety information will be collected by staff at Neufit and EA Therapeutic Health. All personnel involved with patient interactions will have

completed necessary HIPAA training.

Safety data collection will start from recruitment and will be collected at each treatment session. The data, specifically patient health and response to treatment, will be reviewed by the PIs monthly. Research will be suspended if there is any indication of injury or increased pain to participants. Patients will be withdrawn early from the study if there is an indication that they are unable to comply with the protocol or if there are any safety concerns related to side effects of the DC e-stim. Any early withdrawals due to safety concerns will be referred to a physician specializing in rehabilitation medicine for further evaluation

Population and Sample

Inclusion criteria:

1. Must show evidence of axial mechanical low back pain at least 3/10 on visual analog scale, without radiation to the lower limbs. Pain has to have been present for at least two weeks or diagnosed as chronic.
2. Normal lower limb strength
3. Able to attend twice weekly physical therapy visis for up to 6 weeks
4. 18 years of age, or older

Exclusion criteria:

1. Currently pregnant
2. Cardiac pacemaker
3. Active or recently treated cancer
4. Active or recent blood clots
5. Epilepsy
6. Open wounds
7. History of lumbar spine fusion surgery
8. Radicular symptoms suggesting radiculopathy or spinal stenosis.

Participant Recruitment

Participants will be recruited when presenting for an initial physical therapy episode of care to address mechanical low back pain. Physical therapy treatment sessions will be billed to insurance as is the standard of care for this treatment approach. Any patient meeting the inclusion criteria will be told about the study and, if interested, provided with a copy of the informed consent to review. During phone or in person consultation, patients who are interested in joining the study will be required to enroll and submit the signed informed consent form prior to their first study visit. In addition to treatment outcomes, a $50 gift card will be provided to participants upon completion of their treatment sessions and final assessments.

Privacy and Confidentiality

Initial recruitment may occur over the phone, but all additional consent processes and procedures will occur behind closed doors in private treatment rooms with only staff involved in conducting the study present to maximize confidentiality.

Results of this study may be used in publications and presentations. The study data will be handled as confidentially as possible. Individual names and personal identification information will not be collected at any point. Data may be shared for use in future studies or with other researchers. In this case, any personal identifying information of participants will not be included.

Participant data will be stored without any identifiers or codes for 5 years.

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