Neuromuscular electrical stimulation for the treatment of jaw-closing dystonia

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Study Title	Neuromuscular electrical stimulation for the treatment of jaw-closing dystonia
Study Design	6 patients with jaw-closing dystonia will be treated with neuromuscular electrical stimulation over 8 weeks. The distance the mouth can be opened voluntarily, and the oromandibular dystonia questionnaire (OMDQ-25) will be employed to determine whether there is any objective change in jaw opening or evidence of functional improvement.
Primary Objective	(1) Measure whether neuromuscular electrical stimulation increases inter-incisor (or inter-gum) distance in patients with jaw-closing dystonia as an objective measurement of jaw opening. (2) Assess whether neuromuscular electrical stimulation alters quality-of-life in patients with jaw-closing dystonia.
Secondary Objective(s)	(1) Determine effect size, variability and distribution of data to allow rational design of a larger study if the intervention looks promising.
Research Intervention(s)/ Investigational Agent(s)	Omnistim® FX²
IND/IDE #	
Study Population	Adult male and female patients with jaw-closing dystonia
Sample Size	6
Study Duration for individual participants	8 weeks
Study Specific Abbreviations/ Definitions	NMES: neuromuscular electrical stimulation PNES: patterned electrical neuromuscular stimulation PD: Parkinson's disease PSP: progressive supranuclear palsy AD: Alzheimer's disease TDQ: tongue depressor quantity OMDQ-25: oromandibular dystonia questionnaire

Objectives

1. Measure whether neuromuscular electrical stimulation increases inter-incisor (or inter-gum) distance in patients with jaw-closing dystonia as an objective measurement of jaw opening.
2. Assess whether neuromuscular electrical stimulation alters quality-of-life in patients with jaw-closing dystonia.
3. Determine effect size, variability and distribution of data to allow rational design of a larger study.

Background
This pilot study is designed to acquire initial data on whether neuromuscular electrical stimulation might be useful for the treatment of jaw-closing dystonia.

Study design
Open-label pilot study.

Study Primary Endpoints
1. Measure whether neuromuscular electrical stimulation increases inter-incisor (or inter-gum) distance in patients with jaw-closing dystonia as an objective measurement of jaw opening, both before and after each treatment session, and from baseline to the end of the study.

2. Assess whether neuromuscular electrical stimulation alters quality-of-life in patients with jaw-closing dystonia by measuring change in OMDQ-25 from baseline to the end of the study

Study Intervention/Investigational Agent
Omnistim® FX² neuromuscular stimulation device, set to *"muscle spasm reduction"*. The United States Food and Drug Administration has determined that the Omnistim® FX² device is substantially equivalent to other legally marketed predicate devices to be marketed within the provisions of the Federal Food, Drug, and Cosmetic Act.

Procedures Involved
6 patients will be enrolled in the study and written informed consent will be obtained at the beginning of the study prior to the first session.

Each participant will participate in 16 sessions over the 8 weeks of the study.

The electrodes will be placed over bilateral masseters using a bipolar technique; on each side, one electrode will be placed over the motor point, and one electrode will be placed over the belly of the muscle. The Omnistim® FX² device will be set to the *"muscle spasm reduction"* and electrical stimulation will last 20 minutes, during which time the patient will be directly supervised by the treating physician. After completion of stimulation, electrodes will be removed, and the patient's skin will be cleaned and examined for hyperemia and irritation. At

the end of each individual patient session, the equipment will be cleaned with germicidal wipes, including the control panel and lead wires. The electrodes are disposable and will be discarded after singe use.

The severity of jaw-closing dystonia will be measured using 2 methods:

1. Determine how many stacked tongue depressors the patient is able to fit safely between their front incisors (tongue depressor quantity, TDQ). In the case of edentulous patients who are not able to wear their dentures because of dystonia, we will measure the distance between the front gums using the same method. TDQ is a simple rapid measurement that is carried out routinely in speech therapy practice for evaluation and conservative treatment of jaw opening problems. This will be measured before and after each treatment session.
2. The impact of jaw-closing dystonia on the patient's functional status will be determined using the oromandibular dystonia questionnaire (OMDQ-25), which has been shown to be both a valid tool to assess quality-of-life in oromandibular dystonia and sensitive to change after botulinum toxin treatment (Merz et al. 2010). OMDQ-25 will be evaluated at baseline and after each treatment session.

Data and Specimen Banking
All data will be de-identified, with each participant being assigned a study number, and all study documents aside from consent forms will be labeled only with this identifier. De-identified data will be digitized for analysis and stored on a UPMC server in a password-protected user account. There will be no specimen banking.

Sharing of Results with Subjects
Results will be shared with the subjects upon completion of the study.

Study Timelines
Each patient will undergo 16 sessions total, for a total of 8 consecutive weeks (or fewer sessions if individual patients experience discomfort or other problems).

Inclusion criteria:
1. Jaw-closing dystonia, which may be primary or secondary to a neurodegenerative disease or medications.
2. Unable to voluntarily open jaw fully on examination.
3. Evidence of functional impairment resulting from dystonia including inability to completely open the jaw during speaking or eating to such an extent that it interferes with these tasks.
4. Patient interested in participating, and willing to attend multiple treatment sessions in the neurology clinic.

Exclusion criteria:

1. Presence of a cardiac pacemaker, implanted defibrillator, or other implanted electronic device
2. Inability to provide consent (either by the patient, spouse or an identified power of attorney)
3. Age 18 years or younger
4. Pregnancy

Vulnerable Populations

Our study population potentially includes adults with neurodegenerative diseases who may also have cognitive impairment. In the case of severe cognitive impairment that precludes the patient giving *bona fide* informed consent, this will be given instead by the patient's power of attorney (POA), spouse, or adult son or daughter. In this case, treatment will only be carried out with the patient's clear and unequivocal assent. If no POA, spouse, or child is identified, then the patient will be excluded from the study.

Local Number of Subjects

6 patients will be recruited in total for this pilot study.

Withdrawal of Subjects

Patients will be withdrawn from the study if they experience hyperemia at the electrode placement sites that does not resolve between patient sessions, or if they experience more than mild discomfort that requires complete termination of neurostimulation at any point during the course of the study. Patients will also be withdrawn from the study if they experience muscle fatigue or weakness which interferes will daily functions like speaking or chewing food. Placement of a cardiac pacemaker, implanted defibrillator, or other implanted electronic device at any point during the study will also lead to withdrawal.

Risks to Subjects

Prior work using NMES to treat oropharyngeal dysphagia suggests that adverse events can include a burning sensation during treatment, skin irritation and soreness at the electrode site, neck pain, jaw pain, and headache.

Potential Benefits to Subjects

Patients may experience functional improvement in activities impaired by jaw-closing dystonia, including speaking, chewing, mouth opening for oral hygiene, comfort, eating, drinking.

Data Management and Confidentiality

All data collected will be stored in a locked office room and de-identified, with each participant being assigned a study number, and all study documents aside from consent forms will be labeled only with this identifier. A single hard copy key document will relate each participant's identity to their study number. De-identified data will be digitized for analysis and stored on a server in a password-protected user account.

Provisions to Monitor the Data to Ensure the Safety of Subjects
A data and safety monitoring plan will include quarterly meetings to discuss issues regarding enrollment, status of the visits, recruitment, data coding and entry and/or address any adverse events, issues or concerns at that time.

Provisions to Protect the Privacy Interests of Subjects
Research data will be de-identified using a subject number. The only patient identifiable data will be the consent form and the 'key' list relating the participant number to their name, both of which will be stored in a locked filing cabinets in a locked office. Data digitized for analysis will be de-identified and stored in password-protected files on servers in password-protected accounts.

Economic Burden to Subjects
Patients will be given a voucher for free parking to attend study visits.