PROTOCOL TITLE:

Neurophysiological characterization of dry needling in people with spasticity due to stroke--COBRE

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1.0 Objectives / Specific Aims

In individuals post-stroke and other CNS disorders, one of the most common and disabling problems is spasticity (12, 35, 36, 40), which is defined as a velocity-dependent reaction to passive range of motion, and often is demonstrated concurrently with increased resting muscle tone (12, 35-39). In chronic situations, spasticity can lead to secondary changes in spinal and supraspinal pathways (1, 2) and when coupled with muscular weakness these reflex changes can ultimately limit joint motion and impair motor control. Furthermore, when untreated or treated inadequately, spasticity can contribute to increased pain and joint contractures, thereby negatively impacting quality of life (12, 35, 36, 40). Currently, the most common approaches to treat spasticity are pharmacological treatments (12, 3-13) and standard physical therapy (including stretches, massages, and transcutaneous electrical stimulation). Recently, as a potential adjunct to these approaches, an increasing number of physical therapists worldwide have started administering trigger point deep dry needling (DDN) to treat spasticity and associated pain in people with CNS injuries(14-22). Locally, DDN at myofascial trigger points (MTrP) disrupts dysfunctional motor end plates and increases the local blood flow and oxygenation (68, 69) while stimulating nociceptors (60). Conceivably, excitation of nociceptors would influence the excitability of multiple spinal and supraspinal pathways (for example A-β and A-δ (group II/III) sensory afferents (60-64)). To date, the effects of DDN on spinal somatosensory processing are not well understood. To define the clinical utility of DDN in treating spasticity and related sensorimotor disorders, it is essential to understand its neurophysiological impact on CNS pathways. The understanding of the neurophysiological effects of DDN will lead to the optimal use (e.g., timing, amount, and frequency of DDN administration) clinically to ultimately improve the overall quality of life in patients with spasticity secondary to stroke (herein referred to as 'spasticity').

Available small studies, case reports (14-22), and our preliminary data (87) support that DDN likely produces neural plasticity at both spinal and supraspinal levels. Thus, our central hypothesis is that ***DDN at MTrP induces plasticity in the spinal and supraspinal pathways and produces therapeutic effects.*** While the steady increase in therapeutic use of DDN implies its clinical potential, its optimal use is yet to be established, largely due to the limited mechanistic understanding of its neurophysiological effects. This pilot project is our first step towards understanding the neurophysiological mechanisms of DDN, specifically the spinal mechanisms of DDN-induced plasticity. This project evaluates these mechanisms via two specific aims:

Aim 1. **To evaluate the effects of DDN on proprioceptive reflexes in people with spasticity due to stroke.**

In people with spasticity the excitability of the H-reflex pathway (an electrical analog of spinal stretch reflex) becomes elevated and reciprocal inhibition of the plantarflexors by the dorsiflexors becomes impaired (25, 26). Thus, to investigate the effects of DDN at the medial gastrocnemius (MG) MTrP on excitatory and inhibitory proprioceptive reflexes, in 20 individuals with spasticity due to stroke we will measure the H-reflex – M-wave (H/M) recruitment curves and reciprocal inhibition in the triceps surae muscles before, immediately after, 90 minutes after, 24 hours after, and 72 hours after DDN. One week prior to DDN, the same measurements will be repeated 5 times, with inter-measurement intervals matching to pre and post DDN measurements. We anticipate that decreases in H-reflex size and reciprocal inhibition will occur between pre and post DDN time points.

Aim 2. **To evaluate the effects of DDN on cutaneous reflexes in people with spasticity due to stroke.** Modulation of cutaneous reflexes to non-noxious stimulation of the skin become abnormal

post-stroke, reflecting the altered somatosensory processing in this population (33, 34). Thus, in this project, we will examine cutaneous reflex responses to non-noxious stimulation of the distal limb (i.e., at or below the area treated with dry-needling) at the same time points as the proprioceptive reflexes before and after a single DDN session. We anticipate that cutaneous reflex amplitudes will be decreased after DDN.

Additionally, to interpret these reflex changes related to typical clinical measures, we will measure passive and active dorsiflexion range of motion (ROM) and the Modified Ashworth scale, Fugl-Meyer, and 10-m walk test. These measurements will facilitate the development of future DDN clinical trials towards establishing spinal neurophysiological mechanisms of DDN.

The findings from this project would also help clinicians estimate when post DDN motor practice/training therapies should be administered for improving motor function in persons with and without spasticity. The data obtained through this pilot project will significantly strengthen our future NIH R-series applications, through which we plan to test the hypothesis that a single administration of DDN procedures will produce lasting effects on spinal neurophysiology that support temporary relief/alleviation of sensorimotor impairments in people with spasticity due to chronic stroke.

2.0 Background

Sensorimotor disorder after stroke

Spasticity, conventionally seen as increased muscle tone and exaggerated stretch reflexes [12,35-39], is one of the most common and disabling motor control problems after stroke [12,35,36,40]. Together with weakened voluntary muscle contraction [41], it often limits joint movements and results in spastic movement disorders (e.g., circumduction gait). When untreated or treated inappropriately, spasticity may contribute to increased pain and joint contractures, and thereby affect quality of life. Malfunctioning spinal inhibition (including presynaptic inhibition), muscle hypertonus, secondary changes in spinal pathways, and impaired sensory afferent processing and contribution are known contributors to spastic sensorimotor disorders [1,2].

Currently, the most common methods to treat spasticity are pharmacological and physical therapies. Widely applied pharmacotherapy typically disables certain connections (e.g., botulinum toxin) or enhance general inhibition (e.g., baclofen). While its utility has been generally accepted, undesirable side effects may occur [3-13]. Standard methods used in physical therapy, including joint mobilization [42-44] and transcutaneous electrical nerve stimulation [45-47], can also help to reduce spasticity temporally. In recent years, among physical therapists across the US, Europe, and Asia, dry needling has become recognized as a potential alternative tool to treat muscle spasm, spasticity, and pain in people with orthopedic or CNS injuries [16-19,48,49].

Dry needling

As the therapeutic use of dry needling grows, mechanistic understanding of this approach has been building up [21,24,49], although slowly. *Mechanically*, dry needling that targets Myofascial Trigger Points (MTrP) would disrupt dysfunctional motor end plates; that is, needling of MTrPs can stretch the contracted cytoskeletal structures (i.e., shortened sarcomeres) [50] and thereby help to restore the resting level of sarcomere (i.e., muscle fiber) length. Change in the muscle fiber length will then affect the firing of group II muscle spindle afferent, which produces complex effects on the network of spinal inhibitory and excitatory pathways [26,51-54], as well as exciting motoneurons through spinal stretch reflex pathways [55-59].

Physiologically, dry needling stimulates nociceptors (i.e., A-β and A-δ (group II/III) sensory afferents,), which in turn, influences the excitability of multiple spinal pathways (including both excitatory and inhibitory interneurons) [60-64]. This may partly explain pain reduction as a result of

dry needling [19,48,65]. It has been suggested that dry needling also activate serotonergic and noradrenergic systems, which influence the impact of sensory inputs in the spinal dorsal horn [66,67].

Dry needling also affects the local muscle blood flow and oxygen saturation [68,69], which presumably helps to reduce pain-producing substances (e.g., bradykinin, calcitonin gene-related peptide, and Substance P) that are accumulated at/around MTrPs [70,71]. Sustained contractures of taut bands (often felt as palpable contraction knots) cause local ischemia and hypoxia in the MTrPs. Hypoxia, together with myofascial tension, can increase the amount of acetylcholine release at the motor end plate, which can create a self-sustaining vicious cycle of muscle contraction. A drop in pH resulting from low oxygen levels could also excite muscle nociceptors, which sense the peripheral biochemical environment and mediate local blood supply. Sensitized muscle nociceptors have a lower excitation threshold (allodynia) and are more easily respond to muscle movement (mechanical hyperalgesia) [21]. Pain associated with spastic hypertonia can further involve central sensitization. Altered central processing of somatosensory input can be seen in impaired flexor withdrawal reflexes to noxious stimuli and/or impaired cutaneous reflexes to non-noxious stimuli (e.g., [34]). Central sensitization is also the mechanism of referred pain, and involves sensitization and an expansion of receptive fields [21]. For all these reasons, increasing the local blood flow and oxygenation appears to be a key mechanism of action of therapeutic dry needling.

In sum, the current view/presumption is that dry needling can help to restore the functional state of end plate and alleviate hypertonia and hyperalgesia through its immediate mechanical effects on end plate and by increasing the local blood flow and oxygenation. However, to date, its neurophysiological effects on spinal and supraspinal somatosensory processing in people after stroke are not yet understood. To determine the clinical utility of dry needling in treating spasticity and/or related sensorimotor disorders after stroke, it is essential to understand its neurophysiological impact on CNS pathways involved in sensorimotor function. Thus, the goal of this project is to characterize neurophysiological effects of dry needling on spinal and supraspinal somatosensory pathways in people with spasticity due to chronic stroke.

3.0 Intervention to be studied

This project is to examine the neurophysiological mechanisms of trigger point deep dry needling (DDN), a commonly practiced therapeutic method to treat spasticity and pain in individuals with neurological and non-neurological (orthopedic) injuries.

4.0 Inclusion and Exclusion Criteria/ Study Population

Adults (≥18 years old) with spastic hyperreflexia due to stroke.

Inclusion criteria are: 1) neurologically stable for >6 months (and >1 yr post stroke); 2) medical clearance to participate; 3) unilateral ankle and/or wrist spasticity, confirmed by Modified Ashworth Scale (MAS) > 1 and the presence of spastic hyperreflexia, 4) ability to ambulate at least 10 m with or without an assistive device (except for parallel bars). For quantifying hyperreflexia, we will measure the H-reflex in the soleus for the lower extremity. We will enroll post-stroke individuals who exhibit abnormally large H-reflexes [25] and abnormally strong reflex activity during the simple motor task [26,72,73] (e.g., walking and reaching and grasping). The H-reflex is completely suppressed in neurologically normal individuals during the swing phase of walking [74], for example, and therefore, testing reflexes during these dynamic movements is useful for evaluating spasticity.

Exclusion criteria are 1) motoneuron injury (i.e. the neurons that give rise to the axons innervating the muscles) with inadequate response to stimulation; 2) a cardiac condition (history of myocardial infarction, congestive heart failure, pacemaker use, coronary artery disease, atrial fibrillation, congenital heart disease, uncontrolled hypertension); 3) a medically unstable condition

(including temporary infections and pregnancy); 4) age <18 years old; 5) cognitive impairment sufficient to interfere with informed consent or successful completion of the protocol; 6) metal allergies; 7) needle phobias; 8) lymphedema over a limb (due to risk of infection/cellulitis); 9) abnormal bleeding tendencies; 10) compromised immune system; 11) vascular disease; 12) uncontrolled diabetes; 13) history of epilepsy (as DDN generates strong somatosensory sensation); 14) anxiety disorders or in distress; 15) botox injection in targeted muscle within 3 months prior to study procedures.

5.0 Number of Subjects

Twenty adults (≥18 years old) with spastic hyperreflexia due to stroke are recruited from the community around the MUSC and a greater Charleston area.

6.0 Setting

The entire procedures will be performed at the College of Health Professions Research Building on the Medical University of South Carolina campus.

7.0 Recruitment Methods

Adults (≥18 years old) with spasticity due to stroke are recruited from the community around the MUSC and greater Charleston area. Individuals with stroke will be recruited through word of mouth (i.e. support group meetings, through clinicians, health care providers, and participants). Subjects recruited in this manner will be directed to contact the research team directly. This study will also recruit from the Registry for Stroke Recovery (RESTORE-Pro#00037803, IRB approved 9/6/14) which is a research tool sponsored by the National Institutes of Health (NIH) Center of Biomedical Research Excellence (COBRE) in Stroke Recovery with subjects consented for future contact to support stroke recovery research conducted at MUSC. RESTORE staff will query the registry for potential subjects and provide the Principal Investigator (PI) with the contact information of subjects who meet their criteria. The PI or research staff will contact subjects via phone or email to further screen for potential enrollment.

The research coordinator will be the first study staff to make the contact with a potential participant, obtain the medical records, and pre-screen him/her for eligibility. During this process, the coordinator will mail or email the study consent form to the potential participant. For medical/neurological screening of participants, the pre-screened potential participant will be brought to MUSC for an appointment with the study therapist and investigators, if agreed. The coordinator will obtain the signed consent from the potential participant in person, prior to the in-person medical or EMG screening (i.e., first preliminary session).

The participant will be paid $45 for the second and fifth sessions, and $15 for the remaining 5 sessions. S/he will also be provided with transportation reimbursement if needed. The participant will be reimbursed $0.56 per mile for transportation costs for any distance greater than or equal to 1 mile; or if s/he is using a transportation service (CARTA, etc.), the fee may be reimbursed. The payment (including transportation expense) will be made with cash or ClinCard, even if the participant does not complete the sessions.

8.0 Consent Process

At the beginning of each participant's study participation, prior to the medical/neurological screening, the clinical research coordinator will meet a potential participant at MUSC, explain the proposed study, answer questions, and obtain the signed consent in person. The potential participant is encouraged to ask any questions during the consent process and anytime during his/her study participation. If preferred by the potential participant, s/he will directly contact the principal

investigator or co-investigator, for any questions or concerns. Prior to meeting with the coordinator in person, the potential participant will receive a consent form to review and will be given time to discuss this clinical study with anyone (including the PIs of this study) before making a decision.

Individuals with the reduced mental capacity (e.g., due to medication, drug abuse, injury or disease) are excluded from this study (see the fifth exclusion criterion above). Neurophysiological measures to be made in this study require the participant to be able to respond to the investigator's commands and questions during simple motor tasks, and therefore, individuals with known cognitive impairment will be excluded. This further excludes the individual who are not able to consent by him/herself.

Sharing Data: The RESTORE registry (Pro#00037803), from which this study may recruit subjects, also serves as a data analysis tool by which interdisciplinary teams may share data across projects and provide MUSC's stroke recovery research community with a more complete registry with key stroke elements. Some subjects may have participated or will participate in other stroke related research studies at MUSC. Sharing data from this and other stroke research studies with RESTORE will allow for more targeted recruitment efforts in the future and could reduce the burden placed on subjects by reducing the duplicative efforts of collecting common data and physical function assessments requested by multiple studies and storing them in one centralized and secure location.

Subjects are informed in the consent process if they enroll into the RESTORE registry, their data from this study will be shared. Those who have participated in other stroke research will be asked to sign a Release of Study Records form to share data with RESTORE if they did not already authorize release.

Subjects will be asked to sign a HIPAA authorization stating their health information may be disclosed to MUSC investigators requiring their data for their research projects upon approval by an Institutional Review Board.

9.0 Study Design / Methods

This study is a partial cross-over waitlist control design, in which each of the 20 participants post stroke will participate in 7 visits over a two-week period, during which measurements will be taken 10 times. Neurophysiological and functional measurements will be collected five times over 3 visits during the first week (treatment as usual control week), through which each participant will serve as their own "controls" for their second week of measurements. No sham or other treatment procedure will occur during this week. On the second week, all participants will transition to the DDN intervention week where five measurements will be collected over 3 visits (one pre-DDN baseline and four post-DDN measurements: immediately after, 90 minutes, 24 hours, and 72 hours).

Deep Dry Needling (DDN)

DDN procedures used in this project have been widely used in clinical practice to treat spasticity and pain in individuals with neurological and non-neurological (orthopedic) injuries [15,16,18,20,21,48,75].

Each participant receives a single session of DDN, targeting the medial gastrocnemius. In each DDN session, first, localized hypersensitive spots in palpable taut bands of the targeted skeletal muscles (i.e., MTrPs)(75, 76) are identified with pincer palpation. Then, after cleaning the skin area over a MTrPs with alcohol swabs, a disposable stainless steel acupuncture needle is inserted into the skin, penetrating approximately 15 to 20 mm to the depth of the trigger point, until the local twitch response (LTR) is elicited. Once the LTR is confirmed, the needle is moved up and down

(~4-5 mm vertically) with a small piston motions (approximately at 1 Hz for 25 to 30 seconds) with no rotation at the MTrPs (9,10, 38). The same procedure is repeated at other MTrPs in the same local skin region as needed until the LTR is eradicated. After removing the needle, the needled area is rubbed to prevent bleeding and bruising. Each participant will complete 5 repetitions of each of the following: ankle plantarflexion/dorsiflexion passive range of motion (PROM), sub-maximal concentric and eccentric contractions of the plantarflexors as would be typical in a clinical setting.

Electromyography (EMG) and nerve stimulation

At the beginning of each session, surface self-adhesive Ag-AgCl electrodes are placed over the TA, medial and lateral gastrocnemius (MG and LG), and soleus muscles of the studied leg. Throughout the study, all EMG activity is amplified, band-pass filtered (10-1000 Hz), sampled at 3,200 Hz, and stored. Nerve stimulation protocol consists of 4 components: (1) single pulse posterior tibial nerve stimulation for the triceps surae H-reflex / M-wave (H/M) recruitment curve measurement, (2) single pulse common peroneal (CP) nerve stimulation for the TA H/M recruitment curve measurement, (3) multiple pulse (train) tibial nerve stimulation for cutaneous reflex measurement, and (4) multiple pulse (train) superficial peroneal (SP) nerve stimulation for cutaneous reflex measurement.

(1) ***Single pulse posterior tibial nerve stimulation for triceps surae H/M recruitment curve:*** To elicit the triceps H-reflex, the tibial nerve is stimulated in the popliteal fossa, using surface Ag-AgCl electrodes and isolated constant current stimulation. The stimulating electrode pair is placed so as to minimize the H-reflex threshold and to avoid stimulation of other nerves. For eliciting the H-reflex and M-wave, a 1-ms square stimulus pulse is delivered when the participant has maintained his/her natural standing level (typically, 10-20% of maximum voluntary contraction (MVC) level of EMG activity) of soleus EMG activity for at least 2 s. The minimum interstimulus interval is 5 s. An H/M recruitment curve is obtained by gradually increasing the stimulus intensity in increments of 1.2-2.5 mA from the H-reflex threshold to the maximum H-reflex (H_{max}) to an intensity just above what is needed to elicit the maximum M-wave (M_{max}) [77-79], while the participant stands and maintains the above noted level of soleus EMG activity. About 10 different intensities are used to obtain a recruitment curve, and four EMG responses are averaged to measure the H-reflex and M-wave at each intensity. Then, about 100 responses are elicited at the H_{max} level of stimulus intensity (i.e., weak to mild intensity) while monitoring cortical electroencephalographic (EEG) activity.

(2) ***Single pulse common peroneal (CP) nerve stimulation for TA H/M recruitment curve:*** To elicit the H-reflex and M-wave in the TA, the CP nerve is stimulated at the neck of the fibula, using surface Ag-AgCl electrodes and isolated constant current stimulation. For eliciting the H-reflex and M-wave, a 0.5-ms square stimulus pulse is delivered when the participant has maintained his/her natural standing level of soleus EMG activity for at least 2 s, with the minimum interstimulus interval of 5 s. An H/M recruitment curve is obtained by gradually increasing the stimulus intensity from the H-reflex threshold to the H_{max} to an intensity just above what is needed to elicit the M_{max} [77-79], while the participant stands and maintains the above noted level of soleus EMG activity. About 10 different intensities are used to obtain a recruitment curve, and four EMG responses are averaged to measure the H-reflex and M-wave at each intensity. Then, about 100 responses are elicited at the H_{max} level of stimulus intensity (i.e., weak to mild intensity) while monitoring cortical EEG activity.

(3) ***Train of tibial nerve stimulation for cutaneous reflexes:*** The distal tibial nerve is stimulated on the medial surface of the ankle posterior to the medial malleolus by trains of five pulses at 200 Hz, with a pulse width of 1.0 ms [34,80]. The stimulus electrodes are placed at a location at which strong radiating paresthesia is reported by the participant in the appropriate cutaneous

receptive fields (i.e., plantar surface of foot). While standing, the perceptual threshold, defined as the lowest stimulation detectable by the participant, and the radiating threshold (RT), defined as a clear radiating paresthesia, are determined. Perceptual threshold is thought to represent local activation of cutaneous receptors lying immediately underneath the recording electrodes, whereas RT is likely representing electrical activation of fascicles in the underlying cutaneous nerve [80,81]. 1×RT, 2×RT, and 3×RT of train of stimuli are delivered while the standing participant maintains the above described level of soleus EMG activity. Fifteen to 20 trials are averaged for each stimulus intensity, with the minimum inter-train interval of 5s.

(4) ***Train of superficial peroneal (SP) nerve stimulation for the cutaneous reflexes:*** The SP nerve is stimulated on the anterior surface of the leg just near the crease of the ankle joint by trains of five pulses at 200 Hz, with a pulse width of 1.0 ms [34,80]; the stimulus location at which the participant receives strong radiating paresthesia in the appropriate cutaneous receptive fields (i.e., foot dorsum). While standing, the perceptual threshold and the RT are determined. 1×RT, 2×RT, and 3×RT of train of stimuli are delivered while the standing participant maintains the above described level of soleus EMG activity. Fifteen to 20 trials are averaged for each stimulus intensity, with the minimum inter-train interval of 5s.

Analysis of H-reflex and cutaneous reflexes

The H-reflex and the M-wave amplitudes are measured as the peak-to-peak values in time windows determined for each participant. Typically, for the soleus, the H-reflex occurs in a time window of 30–50 ms post-stimulus 6–25 ms post-stimulus for the M-wave. For the MG, LG, and TA, the M-wave and H-reflex occur with shorter latencies [79]. For all muscles, the H_{max}, M_{max}, and H_{max}/M_{max} ratio are obtained from the recruitment curve measurement.

To analyze cutaneous reflexes, the background (prestimulus) EMG is subtracted from the post-stimulus EMG trace [34,78]. Then, subtracted EMG traces from each muscle are analyzed for peak reflex amplitudes at two distinct epochs termed early (~50–75 ms to peak) and middle (~75–120 ms to peak) latencies [78,83].

Assessment of sensory and motor function

Fugl-Meyer Assessment: Fugl-Meyer Assessment is one of the most widely used quantitative measures of motor impairment and recovery in post-stroke hemiparetic individuals. The assessment includes: motor function (upper extremity maximum score = 66; lower extremity maximum score = 34), sensory function (maximum score = 24), balance (maximum score = 14), joint range of motion (maximum score = 44), and joint pain (maximum score = 44). Each item is scored on a 3-point ordinal scale: 0 = cannot perform, 1 = performs partially, 2 = performs fully. The maximum score is 226.

10-meter walk test: The participant is asked to walk at his/her fastest comfortable speed on an indoor flat straight walkway that has markers at 0, 2, 12, and 14 m, 3 times. The 10-meter speed is calculated from when the toes of the leading foot cross the 2-m marker to when they cross the 12-m marker. An assistive device (e.g., walker) can be used. If the participant's device use changes during the study, the measurements will be made with both the new and old devices.

***Modified Ashworth Scale*:** To measure spasticity, resistance to passive movement about a joint is tested at a range of velocities. The score ranges from 0-4 (i.e., 0: normal muscle tone; 4: rigid in flexion or extension [84]).

Visual Analog Scale for Pain: To measure pain, participants rate the level of pain they are experiencing in the affected limb. The score ranges from 0 to 10 (0="no pain" and 10="worst imaginable pain").

Range of Motion: Range of motion in the affected limb is measured using a standard

goniometer. Both passive and active range of motion will be recorded.

10.0 Data Management

Data analysis: Reflex sizes are calculated in reference to each participant's M_{max} measured during natural standing. For example, the peak-to-peak H-reflex amplitude is normalized to the peak-to-peak M_{max} amplitude, and the mean rectified H-reflex amplitude is normalized to the mean rectified M_{max} amplitude.

For comparing reflex sizes before and after dry needling, a two-way repeated measures ANOVA (studied side of the extremity × time) will be used, together with Student t-test with Bonferroni correction as a post-hoc test. For simple comparison between participants without known neurological conditions and participants after stroke (e.g., age and M_{max}), and assessments of changes in sensory and motor function (i.e., only applicable to participants after stroke), a Student t-test will be used.

Data management: The data will be managed by the PIs and research coordinator at the College of Health Professions (CHP). All EMG and assessment data are electronically stored in the secure CHP server with password protection. Only the investigators directly involved in this project have access to these data.

Protection of participant confidentiality is essential in human clinical trials. The participants' confidential information will be securely stored in locked cabinets of a locked room and a password-protected computer, and only the principal and co-investigators and the research coordinator will have access to the participant's confidential information. For the length of the study, limited personal information (specifically, the participant's name, address, and social security number) will also be accessible to the program administrator for processing the participant reimbursement paperwork. Investigators and therapists, who run data collection sessions, will have access to the EMG and other collected data for the purpose of analysis, but will have no access to the participant's confidential information. Alphanumeric codes will be assigned to each participant's dataset to protect confidentiality.

11.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

From the time of initial contact (before obtaining the informed consent for study participation) to the end of project (i.e., study publication), the confidentiality and rights of all the study participants and potential study candidates are protected. At the time of consent, the potential study candidate is assured that s/he has the right to stop participation in any or all parts of the study at any time with no penalty or loss of benefits to which s/he is otherwise entitled.

After the pre-screening, the clinical research coordinator will discard all records of potential study candidates who are not eligible to participate in the study. For candidates after stroke, after the medical/neurological screening (by the study therapist) and the EMG screening, all records of non-eligible candidates will be discarded. For the eligible participants, who will therefore go through the study protocol, the medical, neurological, and personal information will be securely stored in locked cabinets of a locked room and on MUSC's secure network storage, and only the principal and co-investigators and the research coordinator will have access to the participant's confidential information. For the length of the study, limited personal information (specifically, the participant's name, address, and social security number) will also be accessible to the program administrator for processing the participant reimbursement paperwork. Investigators and therapists, who run data collection sessions, will have access to the EMG and other collected data for the purpose of analysis, but will have no access to the participant's confidential information. Alphanumeric codes will be assigned to each participant's dataset to protect confidentiality.

At the time of obtaining consent, the potential participant will be made aware of the fact that

we cannot guarantee the protection of the confidentiality of his/her records, although every reasonable effort will be made to protect it. The consent form will clearly state as "*By law, representatives of the sponsoring organization or other regulatory authorities may inspect these records. All personal information made available for inspection will be handled in strictest confidence and in accordance with data protection laws."*

The coordinator will check with each participant for any discomfort or adverse events that s/he might have experienced after each session. If and when adverse effects or events and any protocol deviations occur, the coordinator or the PI will immediately report them to the department and the IRB.

12.0 Withdrawal of Subjects

- Some of the participants may find DDN to be stressful or painful (e.g., in case of individuals with needle phobias), even after careful screening with the above listed inclusion/exclusion criteria. All participants are assured that they have the right to stop participation at any part of the study procedures.
- DDN is a commonly practiced therapeutic method to treat spasticity and pain in individuals with neurological and non-neurological (orthopedic) injuries. Careful screening with the above listed inclusion/exclusion criteria ensures safe administration of DDN.

13.0 Risks to Subjects

- There is a risk (1-10/100) of local bleeding, hematoma, and needling site pain. In order to minimize this risk, the patient will be placed in a recumbent or comfortable position for the technique and gentle massage/hemostasis will be applied to the needling site post needling [86].
- There is an uncommon risk (1-10/1000) of local or systemic infections or swelling. In order to minimize this risk a clean technique will be utilized with the use of gloves and cleaning the skin around the region with an alcohol swab pre needling [86].
- There is an uncommon risk (1-10/1000) for strong pain during the treatment, nerve irritation, nerve injury, headache, fatigue, vertigo, and nausea. In order to minimize this risk the patient will be placed in comfortable position and will be monitored throughout needling. At any point the subject can request that the needling be discontinued [86].
- There is a rare risk (1-10/10000) for redness, itching, sweating, blood pressure changes, unconsciousness, tachycardia, breathing difficulties, or vomiting. In order to minimize this risk the patient will be placed in comfortable position and will be monitored throughout needling. At any point the subject can request that the needling be discontinued [86].
- There is a very rare risk (<1/10000) for a broken needle. This risk will be minimized by using the appropriate needle and not inserting the needle to the handle of the needle [86].
- There is a very small possibility that the recording and stimulating electrodes will produce minor irritations, such as itchiness. This is extremely unlikely, since the electrodes we use are designed for sleep studies (Vermed., Inc). If itchiness does occur after the experiment, an over-the-counter topical steroid cream will be applied to the skin over which the electrodes were placed. Electrical stimulation of sensory or motor nerves may generate brief non-painful sensations. Careful adjustment of the stimulus intensity and electrode placement should minimize any discomfort.

- There is a risk of loss of confidentiality. From the time of initial contact (before obtaining the informed consent) to the end of the study, every reasonable effort will be made to protect the confidentiality and rights of all the study participants and potential study candidates.
- There is a risk of falling when performing the 10 meter walk test. The participant can use an adaptive device during this assessment, and the risk of falling is no greater than when walking at home or in the community with the same device. The risk of falling will be minimized by study staff, who will walk beside the participant and assist if he/she becomes fatigued or experiences a loss of balance.
- The experimental procedures may have unknown side effects. The researchers will inform study participants if any new side effect is discovered.

14.0 Potential Benefits to Subjects or Others

This study is experimental, and we promise no direct benefits to the study participants. However, some of the participants may benefit from the study intervention (i.e., dry needling). This possibility is supported by several existing studies [14-18,20,48]. Successful completion of this study will help to understand the neurophysiological mechanisms of action resulting from dry needling, which will then help to determine effective uses of this intervention for treating spasticity and related physiological problems in individuals after stroke.

15.0 Sharing of Results with Subjects

This project investigates neurophysiological mechanisms of action of dry needling that has been widely used in therapy clinics across the world, and thus, it is anticipated that to study participants, the immediate clinical value of study results are likely limited. Study results will not be shared directly with the participants.

16.0 Devices

Acupuncture needles used for dry needling will be stored in a locked cabinet in a locked room that can be accessed only by study staff. The physical therapist trained in dry needling will be the only study team member to handle the needles. Each needle is individually packaged in a sterile guide tube that is used to insert the needle into the skin. Following the dry needling procedure, the needle will be disposed of in a sharps container.

References

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