Reliability of measuring voluntary quadriceps activation using the burst superimposition and interpolated twitch techniques

Kimberly N. Frissora

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Reliability of Measuring Voluntary Quadriceps Activation Using the Burst Superimposition and Interpolated Twitch Techniques

by

Kimberly N. Frissora, ATC

Submitted to the Graduate Faculty as partial fulfillment of the requirements for the Master of Science Degree in Exercise Science

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Dr. Abbey Thomas, Committee Chair

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Dr. Brian Pietrosimone, Committee Member

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The University of Toledo

May 2014
An Abstract of

Reliability of Measuring Voluntary Quadriceps Activation Using the Burst Superimposition and Interpolated Twitch Techniques

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Kimberly N. Frissora, ATC

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Objective: To determine the reliability of quantifying quadriceps percent activation of both the burst superimposition stimulation technique (SIB) and interpolation twitch technique (ITT) of stimulation. Additionally, this investigation will identify the reliability of using train and doublet stimuli during both stimulation techniques. Assessment of reliability was conducted over two separate testing sessions spaced one week apart.

Design and Setting: Intraclass Correlation Coefficients (ICCs) were created to assess the reliability of SIB train, SIB doublet, ITT train, and ITT doublet conditions. All data were collected in a research laboratory. Subjects: Sixteen healthy subjects (9 female, 6 male,) participated in this study. Measurements: A Digitimer DS7AH constant current stimulator with a 200 μs max pulse duration (Digitimer Ltd., Hertfordshire, England) and Digitimer DG2A train/delay generator (Digitimer Ltd.), was used for muscle stimulation. Torque data were quantified using a custom-written computer software program (Microsoft Visual Basic, Redmond, WA). Subject-specific maximal current intensities were used during testing. Maximal current was determined by stimulating the quadriceps muscle (SIB) or femoral nerve (ITT) with an individualized intensity not exceeding 400
V and a pulse duration/width of 1000 μs. Individualized intensity was determined at rest, with single pulses of increasing intensity until the torque associated with the electrically evoked muscle contractions reached a plateau and then decreased. During testing conditions (both ITT and SIB) the current that produced the greatest knee extensor torque at rest, plus an additional 20% (typical range of 100 to 400 mA), was given during a maximal quadriceps contraction. An additional 20% was added to that intensity to ensure a supramaximal stimulus during testing. Results: The SIB train showed a poor reliability (ICC = 0.087) while the SIB doublet showed less consistency, with a poor reliability (ICC = 0.349). For the ITT, the train condition also displayed fair reliability (ICC = 0.071) while the ITT doublet had the most dependability, with a strong reliability over the course of the two testing sessions (ICC = 0.312). Conclusions: Ideally, a strong reliability is demonstrated by ICC values of 0.8-1.0. This study determined that none of the techniques or conditions were reliable over the course of the two testing sessions. However, further research must be done in order to determine further reliability of these studies.
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Figure 1 Representation of techniques used to estimate voluntary quadriceps activation. a = peak torque evoked due to the superimposition of the electrical pulses, b = voluntary torque at the time of stimulus delivery, d = stimulus-evoked torque at rest. This figure is taken from Krishnan et al, 2009.
Chapter 1:

Introduction

Voluntary quadriceps muscle activation can be defined as the ability to recruit and modulate muscle activity in order to produce actions that are coordinated and specific to the task being performed.\(^1\) Muscle activation requires the functioning of both the central nervous system (CNS) and peripheral neuromuscular pathways.\(^2\) This voluntary activation and muscle strength, especially in the quadriceps muscles, is essential in relation to physical performance.\(^3\) Failure along either the CNS or the neural peripheral pathways could result in decreased muscle force production.\(^2\) A malfunction of central activation can reduce the muscle output by failing to recruit all necessary motor units for a desired contraction\(^4\) or a reduction in the maximal discharge rate.\(^5\) This decrease in force production can be referred to as central activation deficit (CAD).

Injuries to the knee joint have been shown to result in dysfunction of the quadriceps muscles, which is characterized by weakness and dyskinesia.\(^6\) Muscle inhibition has been found in patients who have suffered from a variety of knee injuries including anterior cruciate ligament (ACL) injuries and subsequent repairs,\(^1\) knee osteoarthritis (OA),\(^6\) total knee arthroplasty, meniscal injuries, and anterior knee pain.\(^7\) Muscle inhibition has also been observed in the contralateral limb following joint injury, specifically in those with knee OA\(^6\) and ACL injuries.\(^8\)

When muscle inhibition results following injury to the joint and persists, CAD becomes known as arthrogenic muscle inhibition (AMI).\(^9\) AMI manifests itself as posttraumatic weakness and can persist long after injury and rehabilitation have finished.\(^10\) AMI prevents the ability of the muscle to activate the motor neurons required
for a muscular contraction by decreasing the neural drive. It is thought that AMI is a protective mechanism, limiting muscle force output to protect the joint from further damage.\textsuperscript{10}

Previous authors have quantified CAD by applying superficial electrical stimulation in conjunction with a voluntary contraction.\textsuperscript{11} The exogenous stimulation activates the muscle fibers which are suffering from the CAD.\textsuperscript{11} When these supramaximal electrical stimulations are provided to a patient’s maximal voluntary isometric contraction (MVIC), the torque produced above the normal MVIC represents motor units that are not able to be volitionally contracted by the patient, and can be seen as a representative of incomplete neural drive to the musculature.\textsuperscript{12} These measurements of voluntary activation can help to indicate incomplete motor unit recruitment and/or suboptimal firing rates among pathological populations.\textsuperscript{12} Currently, there is no gold standard for the measurement of voluntary muscle activation.\textsuperscript{13} However, two forms of muscle stimulation have been used extensively in the literature to produce activation outcomes; the burst superimposition (SIB) technique and the interpolation twitch technique (ITT).

Quadriceps central activation ratio (CAR) has been reliably measured using the SIB technique to determine the nature and the extent of muscle inhibition\textsuperscript{14} and the availability of motorneurons for muscle contraction.\textsuperscript{15} The SIB technique is applied over the quadriceps muscle and utilizes a train of electrical pulses percutaneously during a MVIC of the quadriceps, which temporarily increases the muscle torque output\textsuperscript{14} by recruiting the motorneurons that previously were not voluntarily activated.\textsuperscript{15} This method assumes that the combination of voluntary and stimulated contractions results in full and
complete motorneuron activation, which is difficult to ascertain. With outside factors such as pain, effort, pathological damage etc., MVIC is usually difficult to obtain for pathological patients. Another variable working against this technique is that the skin and other subcutaneous tissues must be penetrated by the electrical stimulus to recruit all of the motorneurons. As the skin and adipose tissues are low in water content, and considered insulators, the intensity of the stimulation that reaches the underlying muscle will vary based on the subcutaneous tissue of the patient.

The second form of stimulation used to measure voluntary muscle activation is ITT, which involves direct stimulation of nerve as opposed to the muscle itself. The goal of the ITT is to directly stimulate the nerve during a voluntary contraction to add an additional action potential to those that are being produced voluntarily. Motor units that are not firing to produce maximal force will then be stimulated and the added action potential will evoke an increase in force from the muscle fibers. It is sometimes reported that the ITT may overestimate muscle activation deficits by its general inability to electrically generate maximal muscle torque, leading to measurement inaccuracies. There are also some methodological issues that arise with ITT, including the timing of the control twitch, the timing of the superimposed twitch, the form of extrapolation that is used, and the type of superimposed stimulus.

As there currently is no gold standard to measuring muscle activation, assessing the reliability of the two most commonly used methods and types, doublet and train application, is imperative to determining the optimal measurement methods of CAD. Reliability, in research, is defined as the degree to which multiple assessments of a subject agree, or are reproducible. A common measure of reliability is the intraclass
correlation coefficient (ICC), which is an appropriate measurement for continuous data, and looks at how closely raters agree with one another for each and every subject.\textsuperscript{18} ICC is the most fitting type of reliability measure to help compare the reliability of the SIB and the ITT over multiple sessions.

**Statement of the Problem**

Central activation deficit of the quadriceps is a true, long-term problem. As quadriceps CAD is present following a plethora of knee joint injuries, it is important to understand the reliability of the two most common methods used to quantify activation deficits, SIB and ITT. Further, it is important to know the reliability of these measures as individuals compare results across the literature that uses both the SIB and ITT techniques.

**Statement of the Purpose**

The purpose of this investigation was to determine the reliability of quantifying quadriceps percent activation of both the SIB and ITT techniques. Additionally, this investigation identified the reliability of using train and doublet stimuli during both techniques.

**Research Hypothesis**

It was our hypothesis that the use of the ITT technique would result in more consistent and reliable measurements over the two testing sessions than the SIB technique will. This is due to the fact that the use of the CAR through SIB stimulation has previously been shown to overestimate activation because of failure of the percutaneous stimulation to correctly activate a quadriceps muscle fibers, leading to a decrease in SIB torque.\textsuperscript{14}
**Limitations**

This study was not without limitation. This study only looked at a healthy population and, therefore, the reliability of these methods only allowed interpretation among healthy individuals. However, reliability of voluntary activation measurements must be established in a healthy population first before it can be established in pathological populations. Additionally, through the use of a healthy population, this research allowed for further investigations to reliably assess changes in voluntary activation. Future research may also be conducted among pathological populations. Similarly, the method deemed more reliable, can be used to critically analyze voluntary activation deficits between multiple investigations utilizing separate methodology.

**Significance of the Study**

This investigation was significant in that understanding the reliability of these methods will allow for interpretation of these techniques used in the literature and help researchers understand the true effect voluntary activation deficits have among pathological populations. The long-term goal was to establish a reliable method for measuring voluntary activation deficits.

**Operational Definitions**

- AMI = **Arthrogenic muscle inhibition**
- CAD = **Central activation deficit**
- SIB = **Burst superimposition**
- ITT = **Interpolated twitch**
- CAR = **Central activation ratio**
- MVIC = **Maximal voluntary isometric contraction**
CNS = Central nervous system

ACL = Anterior cruciate ligament

OA = Osteoarthritis
Chapter Two:
Literature Review

The purpose of this literature review is to explain: 1) voluntary quadriceps activation; 2) quantifying voluntary quadriceps muscle activation; 3) burst superimposition technique; 4) interpolated twitch technique; 5) quantifying activation; 6) limitations of SIB and ITT.

Voluntary Quadriceps Activation

Normal, non-injured knee joint function relies on the activation, strength and endurance of the quadriceps muscles. As these knee extensors are crucial for lower extremity function of normal activities of daily living, evaluating strength in these muscles is an important component of research in patients sustaining knee joint injuries. Knee extension torque is generally measured using a maximal voluntary isometric contraction (MVIC). The voluntary control of muscle strength and endurance can be defined as the ability to recruit and modulate muscle activity in a manner that produces actions that are coordinated and specific to the performed task, referring to the level of neural drive to muscle. As a result, muscle activation requires the functioning of both the central nervous system (CNS) and peripheral neuromuscular pathways.

The CNS processes begin with activation of the motor neuron portions of the cerebral cortex and the motor neuron pool in the ventral grey matter of the spinal cord. Activation of the peripheral neuromuscular pathways starts with action potential transmission along the motor nerve axon, continues along the neuromuscular junction to the muscle membrane and the transverse tubular system, and finally ends with the crossbridge formation of the myosin heads and actin filaments in the muscle. Any sort of failure along either the CNS or the neural peripheral pathways might result in decreased muscle force production. Reduced muscle output occurs due to a malfunction of central
activation and can be either a recruitment failure of all necessary motor units for a desired contraction or a failure of attainment of the maximal discharge rate from the motor units that are recruited. This failure in force production is known as activation deficit.

Central activation malfunctions can reduce muscle output of the quadriceps by failing to recruit all necessary motor units for a desired contraction or a reduction in the maximal discharge rate. This decrease in force production can be referred to as central activation deficit (CAD). The weakness and activation failure that is characteristic of CAD, if persistent, can be termed as arthrogenic muscle inhibition (AMI). AMI is an ongoing reflex inhibition of uninjured musculature surrounding an injured joint that affects the ability of the joint to activate motor neurons for recruitment during a contraction. It is described as a reflexive response to joint injury because it is embedded in the reflexive loop of the neural system, and is beyond a patient’s conscious, voluntary control. An injury, through tissue damage, pain, swelling etc., causes deformation of joint mechanoreceptors, which relay altered afferent information to the CNS. This altered afferent signal is believed to cause inhibition of the motor neurons of the surrounding quadriceps musculature. This shutdown of the musculature, despite its lack of injury, is hypothesized to be a natural response of the body designed to protect the injured joint from further damage. AMI does not allow for full activation of the muscle, thereby restricting force output to theoretically help avoid further aggravation of an injury. The altered information being sent to the CNS comes from mechanoreceptors, such as Ruffini fibers, Pacinian corpuscles, and Golgi-like endings, stimulated because of mechanical deformation caused by damage or distention of the knee capsule. In activation deficits due to unilateral injuries like ACL deficiencies, knee OA, total knee arthroplasty,
meniscal injuries, and anterior knee pain, bilateral activation deficits have been reported. It has been said that the bilateral deficits are due to the CNS mechanisms modulating quadriceps activation in attempt to normalize activation levels between the legs. From an allied health perspective, this information is crucial as it is important for clinicians to effectively treat AMI, since it can result in strength deficits, altered gait patterns in the short-term and after healing has occurred, and the future development of knee OA.

**Quantifying Voluntary Muscle Activation**

Unfortunately, using a MVIC does not provide information that is indicative of the potential magnitude of activation in an individual muscle group. Other authors have previously quantified the failure of central activation by applying superficial electrical stimulation simultaneously with a voluntary contraction. The added exogenous stimulation activates the muscle fibers which are suffering from the activation failure and are not being activated voluntarily and creates a transient increase in torque output. These measurements of voluntary activation can help to indicate incomplete motor recruitment and/or suboptimal firing rates among pathological populations. The two techniques that are generally used to quantify muscle activation are the burst superimposition (SIB) and interpolated twitch techniques (ITT) and can be quantified through the use of either the central activation ratio or percent voluntary activation equations.

**Burst Superimposition Technique**

Quadriceps central activation has previously been reliably measured using the SIB technique. Measuring activation utilizing the SIB technique requires a train of
supramaximal electrical stimuli to be delivered \textsuperscript{15} percutaneously to the quadriceps during the peak of an isometric MVIC that causes a temporary increase in muscle torque output.\textsuperscript{14} The central activation ratio (CAR) is then calculated by dividing the mean knee extension torque during the MVIC by the peak knee extension torque that is generated by the stimulus.\textsuperscript{14} Theoretically, this stimulus recruits any remaining motorneurons that previously have not been voluntary activated.\textsuperscript{15} It also has been used to determine the nature and extent of quadriceps muscle inhibition.\textsuperscript{14}

Because the methodology for the SIB technique often varies widely, it is possible that an inconsistency in the estimation of quadriceps activation is present. Variations in technique include being able to obtain a MVIC from a patient with pain or knee joint damage and the ability of the stimulus to penetrate the insulating skin and adipose tissues of the body.\textsuperscript{15}

**Interpolated Twitch Technique**

The interpolated twitch technique has the ability to facilitate measurement of the central drive to the quadriceps muscle during a MVIC while allowing for accurate determination of maximal voluntary force.\textsuperscript{13} It is able to measure the drive of the motorneurons to the muscle and how that translates into force.\textsuperscript{16} The goal of the ITT is to directly stimulate the involved nerve during a voluntary contraction to add an additional action potential to those that are being produced voluntarily.\textsuperscript{16} If there are motor units that are not firing to produce maximal force the added potential evokes force from the muscle fibers.\textsuperscript{16} Typically, use of the ITT compares the magnitude of the twitch torque evoked at rest with the torque evoked when the stimulus is added to a MVIC.\textsuperscript{13}
Quantifying Activation

The central activation ratio (CAR) equation has previously been deemed a reliable measure when using the SIB technique, determining the nature and the extent of muscle inhibition and the availability of motorneurons. This measurement estimates the overall ability to activate the quadriceps and has been used to document quadriceps CAD. The CAR is calculated by dividing the mean knee extension torque during the MVIC by the peak knee extension torque generated by the superimposed electrical stimulus (Figure 1, Equation 2). In theory, when using any sort of stimulation, if an individual is able to achieve full contraction of all motor units in the quadriceps, the electrical stimulation will not cause a force-producing contraction that is greater than the volitional contraction. Thus, a CAR of 1.0 indicates complete activation of the motorneuron pool and the quadriceps as a whole. In healthy participants, CAR ranges have been previously reported as 0.93–0.99 and 0.95–0.98.

The other commonly used equation for the measurement of muscle activation is the percent voluntary activation equation. Percent activation requires an electrical twitch evoked at rest for normalization purposes. Percent voluntary activation is quantified by expressing the stimulus-evoked torque generated during MVIC as a percentage of the stimulus-evoked torque at rest (Figure 1, formula 1). It has long been recognized by researchers that differences between quantification methods can lead to differences in voluntary activation estimates. In past studies done in healthy, young adults comparing voluntary muscle activation using both CAR and percent activation, estimates derived based on the percent activation were significantly lower than those derived based on CAR. This is thought to be because the electrically evoked torque at
rest is typically lower than maximal voluntary isometric torque used in percent activation and CAR, respectively. These findings were expected, as there is currently no possible method of introducing an electrical stimulus to a patient that reproducibly evokes maximal quadriceps muscle torque.\textsuperscript{17} Based on the equations in figure 1, the CAR approach is likely to overestimate activation to a greater degree than calculating percent activation based on the ITT, because the formula used to derive percent activation from the ITT includes electrically evoked torque in both the numerator and denominator of the quantification equation.\textsuperscript{17} It has also been previously proven that the ITT method of activation can provide insight on peripheral adaptations in muscle, which may present following injury or surgery.\textsuperscript{17}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Representation of techniques used to estimate voluntary quadriceps activation. $a = \text{peak torque evoked due to the superimposition of the electrical pulses, } b = \text{voluntary torque at the time of stimulus delivery, } d = \text{stimulus-evoked torque at rest. This figure is taken from Krishanan et al., 2009}$}
\end{figure}

**SIB and ITT**

As previously mentioned, ITT involves the stimulation of the innervating nerve\textsuperscript{13} while the SIB technique delivers a train of supramaximal electrical stimuli\textsuperscript{15}
percutaneously to the quadriceps muscle. Previous research has compared the two methods and determined that while they produce significantly different results in terms of magnitude, their estimates are both strongly related. However, both methods of stimulation have limitations associated with them. The first is that no consensus among the scientific community has been concluded in regards to the validity of these techniques despite their capabilities. These two techniques both rely on stimuli to be delivered manually at peak torque, and because of this, both experience some measurement error. It is rare for the stimulus to be applied at peak torque, due to the characteristically unsteady nature of MVICs. This can be considered a limitation for both techniques. Another limitation to these techniques may be the amount of underlying adipose tissue to the stimulation areas. A person with a large amount of adipose tissue may present with higher activation values than one without; however, it is possible that the electrical stimulation is not penetrating through the adipose tissue to excite the underlying muscle or nerve. Although each stimulation technique provides a valid estimation of the percentage of motor units able to activate the muscle, both are unable to distinguish what mechanisms are actually causing recruitment failure. Also, neither technique is able to quantify the descending drive to the motorneurons. Lastly, they are both unable to determine whether the firing rates are maximal and cannot take into account the cause of the drive to the motorneurons.
Chapter Three:

Methods

Research Design

Study Design Cross-over study

The independent variables in this study included session number (one and two) and type of stimulation being received (ITT nerve train, ITT nerve doublet, SIB motor point train, and SIB motor point doublet). In addition, pain was assessed for each condition using a standard visual analog scale (Appendix B). Participants between 18-40 years of age were recruited from all races and both sexes, and had a healthy background of no previous injuries/trauma to their lower extremities. The height, body mass, and activity level were recorded for each participant. Participants were excluded if they had a history of: a serious, ligamentous knee injury; a lower-extremity orthopedic surgery of any kind; or a serious, lower extremity trauma in the past 6 months, females who were currently pregnant/breastfeeding, and individuals who had a known heart condition and/or a pacemaker. A serious lower extremity trauma was defined as a fracture in the past six months. We performed all four conditions (ITT nerve train, ITT nerve doublet, SIB motor point train, and SIB motor point doublet) on each participant and used the percent activation equation to quantify voluntary quadriceps muscle activation. Each stimulation type was performed twice, once during the first session and again during the second session, with one week’s rest between sessions. Order of stimulation type was randomized. For this study, the investigator was not blinded. All measurements were taken from the dominant leg in all participants, defined as the limb with which they would kick a ball. In addition, participants filled out a visual analog scale (VAS) to assess
discomfort levels of the electrical stimulating procedures. This study was approved by the Biomedical Institutional Review Board at the University of Toledo, with an IRB number of 108242. Prior to enrolling in the study, each participant signed a statement of informed consent.

**Instrumentation**

During all muscle activation testing, a Biodex System III Pro dynamometer (Biodex Medical Systems, Shirley, NY) was used to measure maximal voluntary torque. During burst superimposition (SIB) testing, two 7 x 13cm DuraStick II® (Chattanooga Group, Hixson, TN) self-adhesive electrodes were used to deliver the stimulus to the quadriceps muscles. A Digitimer DS7AH constant current stimulator with a 200 μs max pulse duration (Digitimer Ltd., Hertfordshire, England) and Digitimer DG2A train/delay generator (Digitimer Ltd.), which is a non-invasive device that delivers electrical stimuli transcutaneously through an electrode attached to skin. The Digitimer DS7AH was approved by the FDA in October 2005. For interpolated twitch (ITT) testing, a 2mm disc, stimulating electrode (EL2524S, BIOPAC Systems Inc) was positioned over the femoral nerve and secured with hypoallergenic tape to provide the stimulus. Torque data were quantified using AcqKnowledge 4.0 software (BIOPAC Systems, Inc., Goleta CA, USA)

**Participant Set-up**

Participants were seated in the Biodex System III dynamometer and positioned in 85° of hip flexion and 90° of knee flexion as measured by a hand held inclinometer. Restrictive straps were secured at the lap and over the shoulders of each participant to control accessory movement during the knee extension task. The tibia, just proximal to the ankle joint, was secured to a pad on the arm of the dynamometer with a Velcro strap.
Participants were instructed to cross arms over the chest during all contractions to avoid unwanted upper extremity involvement in the task.

**Measurements of Quadriceps Voluntary Activation**

Two 7x13cm self-adhesive stimulating electrodes were positioned on the proximal vastus lateralis (with the medial border of the electrode aligned with the anterior superior iliac spine at the height of the greater femoral trochanter) and the distal vastus medialis (with the lateral border of the electrode bisecting the patella 1.5 inches proximal to the superior patellar pole) and were utilized during the SIB technique. For ITT testing, a 2mm disc stimulating electrode (EL2524S, BIOPAC Systems Inc) was positioned over the femoral nerve to provide the stimulus and was secured with hypoallergenic tape.

Following set-up, participants performed a series of warm-up, submaximal isometric quadriceps contractions in which they attempted to extend their knee at 25, 50 and 75% of their self-perceived maximal effort.

Subject-specific maximal current intensities were used during testing. Maximal current were determined by stimulating the quadriceps muscle (SIB) or femoral nerve (ITT) with an individualized intensity not exceeding 400 V and a pulse duration/width of 1000 µs. Individualized intensity was determined at rest, with single pulses of increasing intensity until the torque associated with the electrically evoked muscle contractions reached a plateau and then decreased. The current that produced the greatest knee extensor torque at rest, plus an additional 20% (typical range of 100 to 400 mA), was given during a maximal quadriceps contraction. An additional 20% was added to that intensity to ensure a supramaximal stimulus during testing.
After individualized stimulation intensities were identified, a 2-minute rest period was allowed. Participants then performed three knee extensor maximal contractions for each of the four conditions (ITT train, ITT doublet, SIB train, and SIB doublet) with at least 1 minute of rest between each trial. Individualized intensities were used during all testing conditions; however, specific parameters were used for the doublet (10 µs duration, 100Hz, 10 µs delay) and train conditions (100 µs duration, 10Hz).

During the maximal contraction, the condition specific stimulation (as described above) was given over the quadriceps muscle (SIB) or femoral nerve (ITT) using either the doublet or train condition. Approximately 5 seconds after maximal muscle contraction, a potentiated resting twitch was given for normalization purposes. Each participant was given approximately 2 minutes of rest between testing conditions.

**Visual Analog Scale**

Immediately following the testing period for each of the four conditions, participants were asked to mark their level of pain on a 10cm visual analog scale for pain, ranging from “no pain” to “worst pain imaginable” (Appendix B) This was performed during both testing sessions.

**Data Analysis**

Percent activation was calculated for each trial and the three trials for each testing condition were averaged for analysis (Equation 1).

\[
Percent \ activation = \left[ 1 - \frac{Peak \ torque \ with \ stimulation - MVIC}{Peak \ torque \ of \ potentiated \ twitch} \right] \times 100
\]
Statistical Analysis:

Separate, two-way mixed model intraclass correlation coefficient (ICC) analyses were performed with absolute agreement to determine reliability of the percent activation values over the two data collection time points for each condition. ICC values ≥0.8 were considered strong reliability, ICC values of 0.5-0.79 represented moderate reliability, and ICC values ≤0.49 were considered weak reliability. Paired samples t-tests with an $a$-priori level of $P \leq 0.05$ were performed to determine differences in pain values across conditions within each technique as well as between techniques.
Chapter Four:

Results

Participants

Sixteen participants were initially enrolled in the investigation; however, only data from 14 were available for processing. One participant dropped out before any data could be collected in the first session due to a fear of the measures, and subsequently was unable to be rescheduled. A second participant did not return for his second session. These dropouts lead to a dropout rate of 12.5%. Demographic data for each of the participants can be found in Table 1. Overall means and standard deviations for each condition can be found in Table 2.

Table 1. Participant Demographics

<table>
<thead>
<tr>
<th>Table 1. Participant Demographics</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td>Females</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Height (m)</td>
</tr>
<tr>
<td>Mass (kg)</td>
</tr>
</tbody>
</table>

Burst superimposition train technique

The SIB train technique included 14 valid participant variables and excluded two. The ICC for this condition yielded poor reliability (Table 2) across the sessions. Raw data for each of the SIB train testing sessions can be found in Appendix C and between session scatter plots can be found in Appendix D.
**Burst superimposition doublet technique**

The ICC for the SIB doublet condition was performed including 13 valid variables and excluded three. The results for this ICC yielded poor reliability (Table 2) for SIB doublet across the sessions. Raw data for each of the testing sessions can be found in Appendix C and between session scatter plots can be found in Appendix D.

**Interpolation twitch train technique**

For the train condition of the interpolation twitch technique, the ICC was performed including 13 valid variables and excluding three. This ICC yielded poor reliability (Table 2). Raw data for each testing session can be found in Appendix C and between session scatter plots can be found in Appendix D.

**Interpolation twitch doublet technique**

The ITT doublet condition utilized an ICC and included 11 valid variables and excluded five. This ICC resulted in poor reliability (Table 2). Raw data for each ITT doublet testing sessions can be found in Appendix C and between session scatter plots can be found in Appendix D.

**Table 2. ICC values and Percent activation means and standard deviations**

<table>
<thead>
<tr>
<th></th>
<th>Session 1</th>
<th>Session 2</th>
<th>ICC (95% CI)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>SIB Train</td>
<td>83.074±9.82</td>
<td>86.81±4.74</td>
<td>0.087 (-0.44, 0.57)</td>
<td>0.379</td>
</tr>
<tr>
<td>SIB Doublet</td>
<td>68.94±17.24</td>
<td>72.99±14.98</td>
<td>0.349 (-0.23, 0.75)</td>
<td>0.116</td>
</tr>
<tr>
<td>ITT Train</td>
<td>66.41±23.43</td>
<td>62.92±15.24</td>
<td>0.071 (-0.55, 0.60)</td>
<td>0.411</td>
</tr>
<tr>
<td>ITT Doublet</td>
<td>72.61±9.00</td>
<td>71.12±16.41</td>
<td>0.312 (-0.87, 3.8)</td>
<td>0.807</td>
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</table>

Abbreviations: SIB, superimposed burst; ITT, interpolation twitch technique; ICC, intraclass correlation coefficient; CI, confidence interval
**Visual analog pain scales**

The paired samples t-tests included 12 valid pairs of data comparing SIB train sessions 1 and 2, SIB doublet sessions 1 and 2, ITT train sessions 1 and 2, and ITT doublet sessions 1 and 2. There was also between technique and condition comparisons. Overall means and standard deviations for paired testing can be found in Table 3. Raw data for the VAS values can be found in Appendix E.

Overall, the doublet stimulation parameters produced more pain (greater VAS values) than the train stimulation parameters regardless of SIB or ITT technique. SIB was viewed as more painful than ITT during session two only. Pain during ITT was more variable across sessions, as differences were detected between session one and 2 (Table 3).

Table 3. Visual Analog Scale Pain Responses (data are mean±standard deviation)

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<tr>
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</tr>
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<tbody>
<tr>
<td>SIB Train</td>
<td>2.16 ± 1.66</td>
<td>2.22 ± 1.78</td>
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<tr>
<td>SIB Doublet</td>
<td>3.43 ± 1.87</td>
<td>3.14 ± 1.69</td>
</tr>
<tr>
<td>ITT Train</td>
<td>2.28 ± 1.65</td>
<td>1.26 ± 1.12</td>
</tr>
<tr>
<td>ITT Doublet</td>
<td>3.34 ± 1.60</td>
<td>1.82 ± 1.12</td>
</tr>
</tbody>
</table>

Abbreviations: VAS, visual analog scale; SIB, superimposed burst; ITT, interpolated twitch
*Significantly different from session 1 at $P \leq 0.05$
† Different than train condition for same session at $P \leq 0.05$
‡ Different than ITT train session 2 at $P \leq 0.05$
§ Different than ITT doublet session 2 at $P \leq 0.05$
Chapter Five:

Discussion

The purpose of this study was to determine the reliability of quantifying quadriceps percent voluntary activation for both the SIB and ITT techniques. Additionally, this investigation aimed to identify the reliability of using a train and doublet of stimuli during both techniques. Our results demonstrated that differences in reliability existed between the two widely accepted and commonly used techniques in quantifying quadriceps percent voluntary activation.

Our results demonstrated that all conditions yielded poor reliability between sessions. Overall, this study suggests that muscle activation testing in its present form does not produce reliable measures of voluntary activation over time.

Based on previous research using exogenous stimulation to measure CAD, the burst superimposition technique has been found to be a reliable method in quantifying voluntary activation, as has the interpolated twitch technique. In a study recently published by Grindstaff and Threlkeld, investigators set out to determine the optimal stimulation parameters and methods of calculation for estimating voluntary quadriceps muscle activation while minimizing patient discomfort using both the CAR and percent activation equations with the SIB technique. This study also used both a train and a doublet condition. The results drawn from Grindstaff and Threlkeld’s study suggested the SIB doublet condition produced significantly less superimposed torque than the SIB train condition. Contrary to our findings, Park and Hopkins used CAR and the SIB technique to conduct a similar study looking at between session reliability that resulted in very strong reliability for both variables. Kent-Braun and Le Blanc also conducted a study
that found similar results to those of Park and Hopkins in 1996, stating that the use of SIB train stimuli provides a sensitive measure of the completeness of MVIC, specifically in dorsiflexor muscles and while using the CAR equation.\textsuperscript{5}

It has been suggested by several studies that CAR may overestimate true quadriceps activation,\textsuperscript{14,26} due to the inability of the percutaneous stimulation to adequately activate all of the muscle fibers within the quadriceps muscle.\textsuperscript{26} When comparing the CAR and percent activation calculations, the produced CAR ratios were significantly greater than the values derived using percent activation calculation. However, corroborating our findings, Dousset and Jammes concluded that the SIB technique was not an efficient tool for quantifying central activation failure in regards to their experimental conditions.\textsuperscript{27} The investigators explained that the most evident reason for this conclusion was that central activation failure existed in all participants, but that in some cases, the burst superimposition technique failed to elicit muscle contractions.\textsuperscript{27}

Our results are in disagreement with previously published data which have demonstrated good reliability for these techniques, as well as the train condition being perceived as more painful.\textsuperscript{19,23} The difference in equipment used among the studies could be a possible explanation for these differences. There were several different methods of administering the electrical stimuli. Several previous studies utilized a GRASS stimulator,\textsuperscript{19} while others used a neurostimulator to measure muscle action potentials.\textsuperscript{27} As opposed to the GRASS stimulator, we utilized a Digitimer device. Further, the investigator administering the trials was a novice at using the equipment; therefore the level of experience with the equipment may possibly have affected the results of this study. It is also possible, especially in comparison to Kent-Braun and Le Blanc’s study as
well as Park and Hopkins’ study, that the use of the CAR equation could have played a factor in differences, as we used the percent activation equation. Kent-Braun and Le Blanc also looked specifically at dorsiflexor muscles, not quadriceps muscles, which could also play a role in some of the discrepancies between our studies.

In regards to the VAS of pain, our data showed that pain during ITT testing differed between sessions. In attempting to understand this finding, we examined MVIC data for each session for the ITT testing conditions (train and doublet). We found that the participants generated higher MVIC values during the second compared to the first session (train [session 1: 157.16±69.97 Nm, session 2: 166.53±68.58 Nm, \(P=0.160\)] doublet [session 1: 155.23±70.92 Nm, session 2 171.74±71.94 Nm, \(P=0.032\)]); however, this finding only reached statistical significance for the doublet condition. It is possible that when a participant’s MVIC is higher, he/she is activating a greater proportion of the motoneuron pool. Thus, the stimulus has less motoneurons that it must activate to achieve full activation, which may result in a more comfortable sensation for the participant.

Participants additionally experienced greater pain during delivery of the doublet compared to the train of stimuli. Previous research pertaining to patient discomfort associated with electrical stimuli has shown that pain is variable between participants, and has been described as mild to moderate (3-4 of 10 on VAS). However, other studies have indicated that subjective discomfort levels have been high enough to cause participants to withdraw.\(^{26,28}\) Average results during application of the electrical stimuli in Grindstaff and Threlkeld’s study ranged from 2.2 to 6.7 out of 10 with the doublet pulse, at least 50% less than the train pulse discomfort levels.\(^{26}\) Our results, however, indicate that the doublet was more painful to our participants when compared to the train
parameters. According to Grindstaff and Threlkeld,, the discomfort found during the train condition of his study was slightly higher than has been previously reported.\textsuperscript{26}

The results found in our study differed from previous studies in terms of discomfort. We found that, among our participants, the doublet condition for both the SIB and ITT techniques was significantly more painful than the train stimulation. Raw data from the VAS of this study can be found in Appendix D. Differences between these studies could be attributed to the fact that, for some reason, the train condition was unusually higher in Grindstaff and Threlkeld’s study, making the doublet condition in turn seem less uncomfortable in comparison. Another reason could be that the pain values collected in this study were all relatively low (\textless{}4 on a scale of 10), so the actual differences in discomfort could mean very little clinically.

It is possible that the participants enrolled in this study may have affected the resulting outcomes. Many participants were new to research participation and were hesitant and nervous about receiving electrical stimulation. However this did not appear to be so when looking at VAS pain scales, as average pain reported was no greater than a four for most conditions. There is also a possibility that the participants were not giving their maximal output on each trial, which we tried to compensate for by encouraging them during contractions. Some participants had drastic changes in muscle activation from week to week and others did not. It is possible that participants’ maximal contractions were not truly maximal and were inconsistent week to week depending on the type of stimulation they were about to receive, which can been seen in the raw data in Appendix C. The lack of consistent MVICs is further supported by the t-test results reported above. Participants generated higher MVICs during the second session.
compared to the first, though this finding was only statistically significant during the ITT
doublet testing condition. The lack of consistent MVICs could be due to an anticipation
of being stimulated, or a lack of motivation, despite the encouragement being given from
investigators. All of these factors could have affected the t-test values for the VAS for
pain, which did express differences between techniques and sessions for electrical
stimulation testing. It is also possible that participants did not maintain their same activity
level and nutritional habits across the seven day rest period, which could have accounted
for several factors such as additional muscle soreness and lower MVIC values, or lower
hydration levels, allowing for less percutaneous stimulation to occur. Activity level and
nutritional habits were not recorded during this investigation, which may have affected
outcomes during the second testing session.

Limitations

As with any study, this one is not without limitations. The first limitation of this
study is that participants with a variety of demographics were enrolled. Because our
stimulation techniques are applied percutaneously, varying levels of adipose tissue and
body composition within our participants may have produced variable results. Another
limitation to this study was that during the ITT technique, the participant was instructed
to place the electrode over his or her own femoral nerve. While participants were coached
on how to find the femoral nerve by locating their femoral pulse, we are unable to ensure
the electrode was placed exactly over the nerve. Similarly, the stimulating electrode may
have been placed in varying locations between the sessions separated by a week. In order to
avoid limitations like these in the future, the investigator could apply all electrodes and
stimulating discs. To maintain the same positioning from week to week, pictures could be
taken to document pad positions or they could be marked for the next visit like reported in previous studies.19

**Clinical Relevance**

Being able to quantify quadriceps percent muscle activation can be an important tool in patients suffering from a myriad of knee injuries. Arthrogenic muscle inhibition has been shown to be present after knee injury and can be distinguished by a lack of voluntary quadriceps muscle activation. However, determining the best and most reliable method of quantifying muscle activation is necessary before it can be implemented as a clinical tool. Determining reliability gives clinicians the confidence that the method being used will result in the best possible quantification process.

**Conclusion**

This study attempted to determine the reliability of each of the most commonly used muscle activation quantification techniques, as well as the doublet and train conditions. Looking at the combination of these techniques and conditions, it can be determined that reliability is poor for all techniques and conditions. Further research needs to be done to determine the optimal testing parameters for assessing quadriceps muscle voluntary activation.
References


Appendix A

IRB Consent Form

Adult Research Subject Information and Consent Form
Reliability of Measuring Voluntary Quadriceps Activation

Principal Investigator: Abbey Thomas, PhD, ATC
Other Staff (identified by role): Adam Lepley, MA, ATC (Co-Investigator)
Kimberly Frissora, ATC (Co-Investigator)

Contact Phone number(s): (419) 530-4487

What you should know about this research study:

- We give you this consent/authorization form so that you may read about the purpose, risks, and benefits of this research study. All information in this form will be communicated to you verbally by the research staff as well.
- Routine clinical care is based upon the best-known treatment and is provided with the main goal of helping the individual patient. The main goal of research studies is to gain knowledge that may help future patients.
- We cannot promise that this research will benefit you. Just like routine care, this research can have side effects that can be serious or minor.
- You have the right to refuse to take part in this research, or agree to take part now and change your mind later.
- If you decide to take part in this research or not, and if you decide to take part now but change your mind later, your decision will not affect your routine care.
- Please review this form carefully. Ask any questions before you make a decision about whether or not you want to take part in this research. If you decide to take part in this research, you may ask any additional questions at any time.
- Your participation in this research is voluntary.

Purpose (Why this research is being done):
You are being asked to take part in a research study that looks at how reliable different techniques are at measuring the voluntary activation of your quadriceps (thigh) muscles. The purpose of the study is to examine the reliability between widely used, separate techniques to measure voluntary quadriceps activation. You were selected as someone who may want to take part in this study because you are considered healthy with no previous history of injury to either leg. There will be approximately 40 people participating in this study at the University of Toledo.

Description of the Research Procedure and Duration of Your Involvement
If you decide to take part in this study, you will be asked to report to the Joint Injury and Muscle Activation (JIMA) Laboratory in the Health Science and Human Services building (Room 1409), which is located on the Main Campus of the University of Toledo. You will be asked to come in a total of 2 times (An initial session, followed by a second session exactly 1 week (7 days) later.) Please remember that you can stop participating at any time. If you enroll now and choose not to participate in the follow-up appointment, it will not affect your status at the university. During the sessions, we will test the neuromuscular function of your thigh muscles, which includes two types of electrical stimulation testing, which are described below. Each session will last approximately 1 hour.

**Muscle Activation Testing**

**Type 1: Muscle Stimulation**
You will be asked to sit near the testing chair and two electrodes will be placed on your thigh just like in figure 1. These electrodes will be used to deliver a brief, mild electrical stimulus to your thigh muscles. You will be asked to sit in the testing chair, as seen in figure 2. During the testing session, you will receive a series of submaximal stimulations to determine your individualized stimulation intensity, followed by maximal stimulation trials at your individualized intensity. You will be asked to extend your leg as hard as you can and hold it for five seconds, during which time the electrical stimulus will be delivered to your thigh. The electricity will be approximately a half a second in duration and will contract your thigh muscle for that half-second and relax. Once you are relaxed, an additional stimulation will be delivered to your thigh muscle. You will be asked to perform no more than 5 trials of stimulation to your thigh muscles, and will be allowed up to 1 minute of rest between each repetition.
Type 2: Nerve Stimulation
During this testing, the stimulation is performed with the exact same procedures as above. The only difference is where the stimulation is coming from. During this testing, an electrode will be placed on your upper thigh over top of an underlying nerve, as depicted by the open circle in figure 3. You will be asked to do the same procedures as during muscle stimulation, with the stimulation this time being directed at your nerve. You will be asked to perform no more than 6 trials of stimulation to your nerve, and will be allowed up to 1 minute of rest between each repetition.

![Figure 3](image)

RISKS AND DISCOMFORTS YOU MAY EXPERIENCE IF YOU TAKE PART IN THIS RESEARCH

Likely Risks
- Mild discomfort for a very brief period during the electrical stimulation.
- Mild transient muscle soreness from muscle activation testing.

Less Likely Risks
- Mild, transient skin irritation from the sticky electrodes.

Very Unlikely Risks
- Mild strain to your quadriceps muscle
- Fracture to your patella (knee cap)

RISKS TO UNBORN CHILDREN
It is unknown how the electrical stimulation used in this study would affect an unborn fetus; therefore, if you are, or may be pregnant you will not be allowed to participate in this study.

POSSIBLE BENEFIT TO YOU IF YOU DECIDE TO TAKE PART IN THIS RESEARCH
There are no direct benefits to you for participating in this study. This study is designed so that researchers may learn more about differences in the two different electrical stimulation techniques. This information will be used to develop future studies to improve muscle activity in patients after knee injury.
COST TO YOU FOR TAKING PART IN THIS STUDY
It will not cost you anything to take part in this study. However, you are responsible for providing the means of transportation to the Joint Injury and Muscle Activation Laboratory. You will not be compensated for gas for travel or any other expenses to participate in this study.

ALTERNATIVE (1) TO TAKING PART IN THIS RESEARCH
The only alternative is not to participate in this study.

CONFIDENTIALITY - USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION
By agreeing to take part in this research study, you give to The University of Toledo (UT), the Principal Investigator and all personnel associated with this research study your permission to use or disclose health information that can be identified with you that we obtain in connection with this study. We will use this information for the purpose of conducting the research study as described in the research consent/authorization form.

The information that we will use or disclose includes history of knee joint injury, activity level, and strength or muscle activation measurements. We may use this information ourselves, or disclose this information as part of a research study. Under some circumstances, the Institutional Review Board and Research and Sponsored Programs of the University of Toledo may review your information for compliance audits. We may also disclose your protected health information when required by law, such as in response to judicial orders.

The University of Toledo is required by law to protect the privacy of your health information, and to use or disclose the information we obtain about you in connection with this research study only as authorized by you in this form. There is a possibility that the information we disclose may be re-disclosed by the persons we give it to, and no longer protected. However, we will encourage any person who receives your information from us to continue to protect and not re-disclose the information.

Your permission for us to use or disclose your protected health information as described in this section is voluntary. However, you will not be allowed to participate in the research study unless you give us your permission to use or disclose your protected health information by signing this document.

You have the right to revoke (cancel) the permission you have given to us to use or disclose your protected health information at any time by giving written notice to Dr. Brian Pietrosimone, MB119 2801 W. Bancroft St. Toledo, OH 43606. However, a cancellation will not apply if we have acted with your permission, for example, information that already has been used or disclosed prior to the cancellation. Also, a cancellation will not prevent us from continuing to use and disclose information that was obtained prior to the cancellation as necessary to maintain the integrity of the research study.

Except as noted in the above paragraph, your permission for us to use and disclose your protected health information will stop at the end of the research study. A more complete statement of University of Toledo’s Privacy Practices is set forth in its Joint Notice of Privacy Practices. If you have not already received this Notice, a member of the research team will provide this to you. If you have any further questions concerning privacy, you may contact the University of Toledo’s Privacy Officer at 419-383-3413.

IN THE EVENT OF A RESEARCH-RELATED INJURY
In the event of injury resulting from you taking part in this study, treatment can be obtained at a health care facility of your choice. You should understand that the costs of such treatment would be your
responsibility. Financial compensation is not available through The University of Toledo or The University of Toledo Medical Center. By signing this form, you are not giving up any of your legal rights as a research subject. In the event of an injury, contact Abbey Thomas, PhD, ATC (419) 530-4501.

**VOLUNTARY PARTICIPATION**
Taking part in this study is voluntary. You may refuse to participate or discontinue participation at any time without penalty or a loss of benefits to which you are otherwise entitled. If you decide not to participate or to discontinue participation, your decision will not affect your future relations with the University of Toledo or The University of Toledo Medical Center.

**NEW FINDING**
You will be notified of new information that might change your decision to be in this study if any becomes available.

**OFFER TO ANSWER QUESTIONS**
Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over. If you have questions regarding the research at any time before, during, or after the study, you may contact Dr. Abbey Thomas - (419) 530-4501

If you have questions beyond those answered by the research team or your rights as a research subject or research-related injuries, please feel free to contact the Chairperson of the University of Toledo Biomedical Institutional Review Board at 419-383-6796.
SIGNATURE SECTION (Please read carefully)

YOU ARE MAKING A DECISION WHETHER OR NOT TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES THAT YOU HAVE READ THE INFORMATION PROVIDED ABOVE, YOU HAVE HAD ALL YOUR QUESTIONS ANSWERED, AND YOU HAVE DECIDED TO TAKE PART IN THIS RESEARCH.

BY SIGNING THIS DOCUMENT YOU AUTHORIZE US TO USE OR DISCLOSE YOUR PROTECTED HEALTH INFORMATION AS DESCRIBED IN THIS FORM.

The date you sign this document to enroll in this study, that is, today’s date, MUST fall between the dates indicated on the approval stamp affixed to the bottom of each page. These dates indicate that this form is valid when you enroll in the study but do not reflect how long you may participate in the study. Each page of this Consent/Authorization Form is stamped to indicate the form’s validity as approved by the UT Biomedical Institutional Review Board (IRB).

Name of Subject (please print)          Signature of Subject or Person Authorized to Consent Date

Relationship to the Subject (Healthcare Power of Attorney authority or Legal Guardian)           Time

Name of Person Obtaining Consent (please print)          Signature of Person Obtaining Consent Date

Name of Witness to Consent Process (when required by ICH Guidelines)          Signature of Witness to Consent Process (when required by ICH Guidelines) Date

YOU WILL BE GIVEN A SIGNED COPY OF THIS FORM TO KEEP.

Page 6 of 6
Appendix B

Data Collection Sheets

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**MVIC**

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**Sit Train: Resting Intensity**

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**Sit Doublet: Resting Intensity**

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SIB VAS

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SIB Train

No Pain ————> Worst Pain Imaginable

SIB Doublet

No Pain ————> Worst Pain Imaginable
ITT VAS

Participant #__________ Session: 1 2

ITT VAS: Pain

ITT Train

No Pain ____________ Worst Pain Imaginable

ITT Doublet

No Pain ____________ Worst Pain Imaginable
## Appendix C

### Raw Data: SIB Train

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Appendix D

Scatter Plot between Sessions SIB Train MVIC and RT

SIB Train MVIC

SIB Train RT

45
Scatter Plot between Sessions SIB Doublet MVIC and RT

**SIB Doublet RT**

- X-axis: Session 1
- Y-axis: Session 2
- Data points show a positive correlation

**SIB Doublet MVIC**

- X-axis: Session 1
- Y-axis: Session 2
- Data points show a positive correlation
Scatter Plot between Sessions ITT Train MVIC and RT

ITT Train MVIC

ITT Train RT
Scatter Plot between Sessions ITT Doublet MVIC and RT

ITT Doublet MVIC

ITT Doublet RT
### Appendix E

**Raw Data: Pain Visual Analog Scale**

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