TRANSLATIONAL PHYSIOLOGY

Intermittent electrical stimulation redistributes pressure and promotes tissue oxygenation in loaded muscles of individuals with spinal cord injury

Selina Gyawali,1 Leandro Solis,2 Su Ling Chong,1 Cara Curtis,3 Peter Seres,4 Isaak Kornelsen,3 Richard Thompson,4 and Vivian K. Mushahwar1,3

1Centre for Neuroscience, Faculty of Medicine and Dentistry; 2Rehabilitation Sciences Program, Faculty of Rehabilitation Medicine; 3Department of Cell Biology, Faculty of Medicine and Dentistry; and 4Peter S. Allen MR Research Centre, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

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Gyawali S, Solis L, Chong SL, Curtis C, Seres P, Kornelsen I, Thompson R, Mushahwar VK. Intermittent electrical stimulation redistributes pressure and promotes tissue oxygenation in loaded muscles of individuals with spinal cord injury. J Appl Physiol 110: 246–255, 2011. First published September 30, 2010; doi:10.1152/japplphysiol.00661.2010.—Deep tissue injury (DTI) is a severe form of pressure ulcer that originates at the bone-muscle interface. It results from mechanical damage and ischemic injury due to unrelieved pressure. Currently, there are no established clinical methods to detect the formation of DTI. Moreover, despite the many recommended methods for preventing pressure ulcers, none so far has significantly reduced the incidence of DTI. The goal of this study was to assess the effectiveness of a new electrical stimulation-based intervention, termed intermittent electrical stimulation (IES), in ameliorating the factors leading to DTI in individuals with compromised mobility and sensation. Specifically, we sought to determine whether IES-induced contractions in the gluteal muscles can 1) reduce pressure in tissue surrounding bony prominences susceptible to the development of DTI and 2) increase oxygenation in deep tissue. Experiments were conducted in individuals with spinal cord injury, and two paradigms of IES were utilized to induce contractions in the gluteus maximus muscles of the seated participants. Changes in surface pressure around the ischial tuberosities were assessed using a pressure-sensing mattress, and changes in deep tissue oxygenation were indirectly assessed using T2*-weighted magnetic resonance imaging (MRI) techniques. Both IES paradigms significantly reduced pressure around the bony prominences in the buttocks by an average of 10–26% (P < 0.05). Furthermore, both IES paradigms induced significant increases in T2* signal intensity (SI), indicating significant increases in tissue oxygenation, which were sustained for the duration of each 10-min trial (P < 0.05). Maximal increases in SI ranged from 2–3.3% (arbitrary units). Direct measurements of oxygenation in adult rats revealed that IES produces up to a 100% increase in tissue oxygenation. The results suggest that IES directly targets factors contributing to the development of DTI in people with reduced mobility and sensation and may therefore be an effective method for the prevention of deep pressure ulcers.

Deep tissue injury; electrical stimulation; spinal cord injury; MRI; oxygenation

PRESsURE ULCERS are a highly prevalent complication associated with immobilization or loss of sensation. Populations at risk of developing ulcers include the elderly; people with neurological insults, cancer, bone and joint disease, diabetes, or cardiovascular failure; and those undergoing surgery. Beyond the burden on health and quality of life, the costs to the health care system are enormous. In North America alone, the annual cost of treating pressure ulcers that develop during a hospital stay is $2.2 to $3.6 billion (68).

Deep tissue injury (DTI) is a newly recognized form of pressure ulcer that originates at deep bone-muscle interfaces and progresses outward unbeknownst to the afflicted individual or caregiver (44, 50, 67). Entrapment of soft tissue between bony prominences and an external surface is the primary cause of DTI (15) and leads to muscle breakdown due to sustained mechanical deformation and ischemia-reperfusion injury (1, 22, 45, 61). These pressure ulcers are severe wounds that often necessitate dramatic interventions such as surgical reconstruction or amputation and can require months of hospitalization to manage (48). Furthermore, DTI can be fatal: on average, 8% of individuals who require hospitalization for their pressure ulcers die of related complications such as sepsis (47, 48, 62).

While noted in humans as early as 1975 in a classical paper by Shea (56), who observed DTI-like lesions in people with spinal cord injury (SCI), clinical awareness of DTI has only recently been achieved. Furthermore, there are presently no clinically viable methods for the early detection of DTI, although investigations in this area are under way (28). Development of means for the prophylactic prevention of DTI is of paramount importance.

Current pressure ulcer prevention methods involve the use of pressure-reducing surfaces and weight-shifting paradigms. Despite substantial improvements in these approaches over the years, the incidence of pressure ulcers has not been effectively reduced (11, 20, 21, 30, 46, 51, 54, 63). Moreover, conventional prevention methods have focused on reducing pressure at the seating surface; however, the prevention of DTI requires frequent redistribution of pressure and soft tissue deformation at the bone-muscle interface. To this end, we proposed the use of a novel intermittent electrical stimulation (IES) paradigm (Fig. 1A) that periodically produces muscle contractions. The resulting postural shifts resemble the subconscious movements performed by able-bodied individuals in response to discomfort while sitting. In addition to the dynamical redistribution of pressure, long-term use of electrical stimulation can improve tissue viability by reducing muscle atrophy and improving circulation and transcutaneous oxygen (3–6, 16, 31).
Previously, we showed that IES can prevent DTI in the loaded and persistently deformed tissue of a rodent model of pressure ulcers (57). A pilot study in able-bodied volunteers further demonstrated that IES administered to the gluteal muscles induces significant reductions in surface pressure and increases in tissue oxygenation in the loaded buttocks of seated individuals (58, 59).

The main goal of the present study was to investigate the IES-induced changes in pressure and deep tissue oxygenation in individuals with SCI. Pressure ulcers are one of the most common secondary complications faced by people with SCI (2, 26, 29, 35, 42, 65, 66) and are a leading cause of rehospitalization (8, 14, 25, 38, 53). It is estimated that 80% of people with SCI develop at least one pressure ulcer during their lifetime (51), and 91% of those are at risk of developing a recurring ulcer (41). This makes SCI an appropriate model population for assessing the pressure ulcer prevention effects of IES.

**METHODS**

All experimental protocols were approved by the Human Ethics Committee at the University of Alberta, and participants provided informed consent. Each volunteer participated in two sessions, one assessing the effects of an IES paradigm on surface pressure while seated, and another assessing the effects of the same paradigm on tissue oxygenation in the gluteus maximus muscles.

**Participants**

Seventeen individuals with SCI qualified for the study. Participant characteristics are summarized in Table 1. Exclusion criteria included 1) existing ulcers in the pelvic region, 2) denervated gluteus maximus muscles (a condition commonly encountered in injuries lower than the thoracic 9 vertebral level, resulting from the death of motoneurons innervating muscles of the lower extremities), and 3) contraindications for use of magnetic resonance imaging (MRI) such as metal implants or implanted drug infusion devices.

**Electrical Stimulation**

At the beginning of each session, a research physiotherapist located the motor points for the gluteus maximus muscles bilaterally using a custom, sliding electrode. A two-channel stimulator (BioMedical Life Systems, Vista, CA) was used to administer current (biphasic, cathodic-first, charge-balanced pulses, 200 µs in duration and 40 Hz frequency) to the gluteus maximus muscles. The threshold amplitude eliciting a minimal contraction and the amplitude producing a maximal contraction were determined. Pairs of nonmagnetic, 50 mm × 100 mm surface electrodes (PureCare, Sherwood Park, AB, Canada) were placed bilaterally on the gluteus maximus muscles with the cathode over the motor point and the anode positioned rostrally along the muscle. Stimulus amplitudes producing maximal contractions were used.

**IES Paradigms**

The main IES pattern consists of a short “ON” phase (~10 s long) during which electrical stimulation is administered to induce a concurrent contraction in the gluteus maximus muscles. This brief “ON” period is followed by a substantially longer “OFF” phase (~10 min long) during which no stimulation is administered and the gluteal muscles relax. Two IES paradigms were investigated in this study: 1) continuous stimulation, in which the “ON” phase of IES consisted

**Table 1. Participant characteristics**

<table>
<thead>
<tr>
<th>Volunteer</th>
<th>Age</th>
<th>Sex</th>
<th>Weight, lbs</th>
<th>Level of Injury</th>
<th>Type of Injury</th>
<th>Extent of Impairment</th>
<th>Year of Injury</th>
<th>IES Paradigm</th>
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<tbody>
<tr>
<td>A</td>
<td>40</td>
<td>F</td>
<td>122</td>
<td>T4-T5</td>
<td>SCI</td>
<td>Complete</td>
<td>1999</td>
<td>Continuous</td>
</tr>
<tr>
<td>B</td>
<td>32</td>
<td>M</td>
<td>164</td>
<td>C1-C2, T3</td>
<td>SCI</td>
<td>Complete</td>
<td>2006</td>
<td>Continuous</td>
</tr>
<tr>
<td>C</td>
<td>30</td>
<td>M</td>
<td>171</td>
<td>C4</td>
<td>SCI</td>
<td>Complete</td>
<td>2003</td>
<td>Continuous</td>
</tr>
<tr>
<td>D</td>
<td>33</td>
<td>F</td>
<td>130</td>
<td>C6-C7</td>
<td>SCI</td>
<td>Complete</td>
<td>2007</td>
<td>Continuous</td>
</tr>
<tr>
<td>E</td>
<td>66</td>
<td>M</td>
<td>208</td>
<td>T4</td>
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<td>Continuous</td>
</tr>
<tr>
<td>F</td>
<td>31</td>
<td>F</td>
<td>135</td>
<td>C6-C7</td>
<td>SCI</td>
<td>Complete</td>
<td>2007</td>
<td>Continuous</td>
</tr>
<tr>
<td>G</td>
<td>32</td>
<td>M</td>
<td>150</td>
<td>C6-C7</td>
<td>SCI</td>
<td>Complete</td>
<td>2001</td>
<td>Continuous</td>
</tr>
<tr>
<td>H</td>
<td>22</td>
<td>M</td>
<td>165</td>
<td>C5-C6</td>
<td>SCI</td>
<td>Complete</td>
<td>2005</td>
<td>Continuous</td>
</tr>
<tr>
<td>I</td>
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<td>C5</td>
<td>SCI</td>
<td>Complete</td>
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</tr>
<tr>
<td>J</td>
<td>31</td>
<td>M</td>
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<td>C6-C7</td>
<td>SCI</td>
<td>Complete</td>
<td>1999</td>
<td>Bursting</td>
</tr>
<tr>
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<td>M</td>
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<td>Complete</td>
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<td>Bursting</td>
</tr>
<tr>
<td>L</td>
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<td>SCI</td>
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<tr>
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<td>M</td>
<td>189</td>
<td>C3-C4</td>
<td>SCI</td>
<td>Complete</td>
<td>1987</td>
<td>Bursting</td>
</tr>
<tr>
<td>N</td>
<td>35</td>
<td>F</td>
<td>172</td>
<td>C5</td>
<td>SCI</td>
<td>Complete</td>
<td>2003</td>
<td>Bursting</td>
</tr>
<tr>
<td>O</td>
<td>25</td>
<td>F</td>
<td>NA</td>
<td>T5</td>
<td>SCI</td>
<td>Complete</td>
<td>2000</td>
<td>Bursting</td>
</tr>
<tr>
<td>P</td>
<td>31</td>
<td>F</td>
<td>135</td>
<td>C6-C7</td>
<td>SCI</td>
<td>Complete</td>
<td>2007</td>
<td>Bursting</td>
</tr>
<tr>
<td>Q</td>
<td>53</td>
<td>M</td>
<td>139</td>
<td>C7-T1</td>
<td>Nontraumatic SCI</td>
<td>Incomplete</td>
<td>2003</td>
<td>Bursting</td>
</tr>
</tbody>
</table>

Participant characteristics for the 17 individuals who took part in the study. M, male; F, female; SCI, spinal cord injury; C, cervical; T, thoracic; NA, not available.
of bilateral gluteal stimulation for either 7 or 13 s (Fig. 1B), followed by a 10 min “OFF” phase; and 2) bursting stimulation, during which three bursts of stimuli were delivered bilaterally to the gluteus maximus muscles, each 3 s long with a brief 2-s rest period between (Fig. 1C). This also was followed by a 10-min “OFF” phase. The two paradigms were chosen to investigate the mechanism by which IES generates increases in oxygenation. It was anticipated that the continuous paradigm would increase oxygenation by the influx of blood to the contracting tissue via reactive hyperemia, while the bursting paradigm would act as a “muscle pump” to increase oxygenation.

The 17 volunteers were randomly assigned to one IES paradigm. Nine individuals were assigned to the continuous and eight to the bursting stimulation groups. Participants in the continuous stimulation group received both the 7- and 13-s durations of “ON” phase of IES to investigate the effects of stimulation duration on the benefits produced by the induced contractions.

**Surface Pressure Measurements**

Ideally, assessing an intervention to prevent DTI would measure the reduction in tissue loading and deformation at the bone-muscle interface. Currently, only invasive or indirect methods of measuring internal pressure changes exist. The invasive methods, including the use of pressure-sensing catheters, are unsuitable for use in human volunteers. However, indirect methods such as MR tagging, in which the displacement of tag lines allows one to calculate internal strain and deformation, could be utilized to measure how IES affects internal strain and pressure in future studies. These analyses were beyond the scope of the present study.

In the present study, surface measurements of pressure were used to indirectly assess changes in pressure around the ischial tuberosities (ITs) during IES. The effect of each IES protocol on superficial pressure was tested by seating the volunteers on a Jay 2 composite gel/foam wheelchair cushion (Sunrise Medical, Longmont, CO). A pressure-sensing mattress composed of a 36 x 36 array of 1-cm² pressure sensors (XSENSOR, Calgary, AB, Canada) was placed over the wheelchair cushion. Pressure maps were obtained during periods of sitting at rest, and during contractions induced by IES.

Each IES paradigm was repeated two to four times. A replicate consisted of the acquisition of a 5-s period of rest (baseline) followed by the “ON” phase of IES (contraction). Pressure recordings were sampled at a rate of 10 frames/s and subsequently imported into Matlab (Mathworks, Natick, MA) and analyzed using custom-written programs. A trial-by-trial inspection was conducted to ensure that the magnitude of the contraction remained consistent throughout the testing session.

For each volunteer, the pressure recordings per sensor were pooled across trials within an IES paradigm for the baseline period and “ON” phase of IES. For example, for the continuous bilateral IES paradigm with a 7-s “ON” phase, the pressure recordings from each sensor during the 5-s period of baseline were pooled across trials, as were the measurements from each sensor during the “ON” phase. Therefore, for the two to four trials in this paradigm, 100–200 data points were acquired per sensor during the baseline period and 140–280 data points per sensor during the “ON” phase. The difference in pressure values between the baseline and “ON” phase were then compared to provide a paradigm-specific, sensor-by-sensor spatial distribution of the pressure changes induced by IES. The pressure changes localized around the ITs were then calculated as a percent change from baseline values and averaged across all participants.

**Oxygenation Measurements**

T₂*-weighted MRI scans were used to assess tissue oxygenation within the gluteus maximus muscles. This blood oxygen level dependence (BOLD) imaging approach for assessing changes in muscle tissue oxygenation has been previously used (13, 36, 64). Briefly, BOLD effects are utilized to estimate the level of tissue oxygenation by assessing the intensity of the T₂* signal. The rate of decay of the T₂* signal is affected by the concentration of deoxyhemoglobin, i.e., the presence of deoxygenated blood. Relative increases in deoxygenated blood result in increases in the rate of signal decay. This decay can be measured as decreases in T₂* signal intensity (SI) (43). Thus the changes in SI can be quantified to provide an indirect measurement of deep tissue oxygenation based on the relative levels of oxyhemoglobin to deoxyhemoglobin (23, 36, 37).

All trials took place at the Peter S. Allen MR Research Centre at the University of Alberta, using a 1.5-T whole body scanner (Sonata, Siemens Medical Solutions, Erlangen, Germany). Due to the limited space inside the magnet a custom-built, MRI-compatible chairlike apparatus was used to simulate the pressures experienced in the gluteal muscles during sitting (Fig. 2A). An adjustable indenter and neoprene sheath allowed variable levels of loading to be applied against the gluteal muscles and ITs. Directly before scanning, a "ON" phase of IES (contraction). Pressure recordings were sampled at a rate of 10 frames/s and subsequently imported into Matlab (Mathworks, Natick, MA) and analyzed using custom-written programs. A trial-by-trial inspection was conducted to ensure that the magnitude of the contraction remained consistent throughout the testing session.

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![Fig. 2. Set-up for simulating sitting pressures in a horizontal MR scanner. A custom-built apparatus (A) was used to simulate sitting pressure profiles around the ischial tuberosities in each participant (B). The apparatus consisted of an adjustable indenter used to compress the gluteal muscles and recreate a sitting pressure profile inside the magnet (C).](http://jap.physiology.org/.../image)
pressure profile of each volunteer was obtained while they were seated upright in a standardized wheelchair. After transfer to the scanning apparatus, the indenter and sheath were positioned to recreate this profile (Fig. 2, B and C). Furthermore, visual comparison of MRI scans from the present study with scans obtained in sitting individuals using an open MRI scanner (32, 55) suggest that both modes of loading produced very similar tissue deformations. The matching in superficial pressure and tissue deformation profiles between actual and simulated sitting ensured that any changes in tissue oxygenation produced by IES in the magnet would replicate the changes that occur when seated in a wheelchair.

Each T2*-weighted imaging trial consisted of a 30-s baseline period, the “ON” phase of IES, and a poststimulation period of 9 min and 20 s (“OFF” phase of IES). A two-element spine array coil combined with a two-element flexible coil (CP Body Array Flex, Sonata, Siemens Medical Solutions, Erlangen, Germany) were used to image the pelvic and upper thigh region. The T2*-weighted scan parameters were echo time = 37 ms, repetition time = 1,330 ms, number of slices = 15, slice thickness = 6 mm, slice separation = 12 mm, field of view = 400 mm × 275 mm, readout matrix = 88 pixel × 128 pixel, in-plane resolution = 3.1 mm × 3.1 mm. The 15 slices provided coverage of the pelvic and upper thigh region; 450 sets of these slices were acquired over 10 min.

Temporal changes in tissue oxygenation due to IES. For each paradigm, two to four trials were obtained and averaged per person. The resulting images were analyzed using custom-written Matlab programs. Of the 15 slices obtained, 8 containing the entirety of the gluteus maximus muscle were used for analysis. A region of interest (ROI) was selected around the right and left gluteus maximus muscles in each slice, and the SI was determined. The average precontraction SI value was calculated over the 30-s baseline period, and subsequent values were normalized to this value. The SI values were averaged into 30-s bins and expressed as a percentage change relative to baseline.

Spatial changes in tissue oxygenation due to IES. A slice-by-slice analysis was completed to determine if spatial differences in oxygenation levels throughout the muscle existed relative to the tissue most deformed by the ITs. The SI values in the ROI for each of the eight slices were assessed pre- and post-IES and collapsed over time to represent the overall change in oxygenation in each slice.

Statistical Analysis

Paired t-tests were used to compare the percent changes in pressure produced by the IES paradigms relative to baseline in each volunteer. Group changes were compared to each other using a one-way ANOVA and Tukey’s honestly significant difference (HSD) post hoc analysis. Similarly, changes in oxygenation due to the IES paradigms were compared to baseline values and each other using a one-way ANOVA and Tukey’s HSD post hoc analysis. Differences were considered to be significant for P ≤ 0.05. All results are presented as means ± SE.

Direct, Invasive Assessments of Tissue Oxygenation in Rats

Experiments were conducted in six adult female Sprague-Dawley rats (250–350 g) to further investigate the changes in tissue oxygenation due to IES and correlate them to T2*-weighted measurements obtained in human volunteers. All protocols were approved by the Animal Care and Welfare Committee at the University of Alberta.

The experiments focused on verifying the IES-induced pattern of SI changes seen in human volunteers and correlating the magnitude of the changes to direct measures of tissue oxygenation using invasive assessment. A combination of contraction strengths (moderate, maximal) and loading levels (18, 28, and 38% of body weight) were assessed.

Experimental setup. The rats were anesthetized with sodium pentobarbital as described elsewhere (57). Surgical-plane anesthesia level was maintained throughout the experiment. IES was administered to the gastrocnemius muscle of one hindlimb via a bipolar cuff electrode implanted around the tibial nerve.

The rats were placed in an MR-compatible, custom-built apparatus in a prone position. The foot of the experimental hindlimb was placed in a plaster boot, rotated medially, and secured at the ankle. This pushed the gastrocnemius muscle into an accessible position and ensured an isometric contraction during stimulation. An indenter (3-mm diameter) loaded the gastrocnemius muscle around the midline and approximately one-third of the distance from the knee to ankle joint. The indenter served as the IT, and the tibia acted as the external seating surface, effectively loading the soft tissue in a manner similar to that seen in the seated human condition (57).

Verification of signal intensity in T2*-weighted images. Changes in SI due to IES were assessed using an MR protocol similar to that in the human study. After the gastrocnemius muscle was loaded, MR images were obtained while utilizing IES to induce a maximal contraction. Stimulation consisted of biphasic, cathodic-first, charge-balanced pulses, 200 μs in duration, delivered through the nerve cuff.

A 3-cm birdcage coil (Siemens Medical) was used to image the rat’s hindlimb. Each trial consisted of a 30-s baseline period, a 10-s “ON” phase of IES, and a 15-min “OFF” phase. T2*-weighted image parameters were echo time = 25 ms, repetition time = 500 ms, number of slices = 5, slice thickness = 3 mm, slice separation = 3.6 mm, field of view = 55 mm × 19 mm, readout matrix = 44 pixel × 128 pixel, in-plane resolution = 0.43 mm × 0.43 mm. A total of 1,200 sets of slices was acquired over the 15-min trials. The five slices covered the length of the gastrocnemius muscle. The SI in the gastrocnemius muscle following the IES-induced contraction in all slices was compared with that during baseline.

Correlation of T2* signal intensity to direct measurements of tissue oxygenation. Changes in tissue oxygenation due to IES were directly measured using an oxygen sensor (Oxylite, Oxford Optronix, Oxford, UK) inserted into the gastrocnemius muscle. The sensor was positioned parallel to the long axis of the muscle and situated adjacent to the indenter.

The level of muscle loading (18, 28, and 38% of body weight) and strength of IES-induced contractions (maximal and moderate) were manipulated between trials to observe their effects on tissue oxygenation. Trials consisted of the same protocol used in the MRI tests, and oxygen readings were obtained every 5 s and digitized at a rate of 10 samples/s using a data-acquisition interface and associated software (Power 1401 and Signal 2.13; Cambridge Electronic Design, Cambridge, UK).

RESULTS

IES Redistributes Surface Pressure in the Atrophied Muscles of Seated Human Volunteers with SCI

Examples of baseline pressure profiles obtained during rest in seated volunteers and during the “ON” phase of IES are shown in Fig. 3, A and B, respectively. IES-induced contractions in the atrophied muscles produced a reduction in pressure over the IT region that was accommodated by an increase in pressure in tissue away from the ITs. Both IES protocols (continuous and bursting) produced a consistent pattern of significant pressure reductions over the ITs (1-way ANOVA, P < 0.05) (Fig. 3C).

The average range of pressure reduction over the ITs relative to baseline across individuals and IES paradigms was 10–26% with reductions up to 100% seen in some individuals. The variability in the range of reduction resulted primarily from the use of a pliable wheelchair cushion, and secondarily, from the amount of adipose tissue present in each volunteer. Both factors affected the levels of pressure...
measured by the sensors within the pressure mattress. Therefore, the interaction of the cushion and the changing shape of the buttocks during the contractions introduced a level of variability in the measured superficial pressures, an experimental artifact that could not be removed in this study. Nonetheless, the reductions in superficial pressure around the ITs were consistently present in all volunteers.

A summary of the average percent reduction in pressure for both the left and right sides of the buttocks is shown in Fig. 4. Within the continuous paradigm, the 13-s protocol produced 9.8 ± 5.9% and 10.2 ± 5.6% reductions in pressure on the left and right sides, respectively, and the 7-s protocol produced reductions of 10.3 ± 5.1% and 22.3 ± 12.7%. The bursting paradigm produced 20.5 ± 10.2% and 26.3 ± 14.4% reductions on the left and right sides, respectively. While it is unclear why differences in pressure reduction were observed between the left and right sides, similar differences were observed in able-bodied volunteers. The differences may be related to unbalanced sitting that could not be corrected or volunteer handedness. All IES-induced reductions were significant (P < 0.05), except for 13 s, left side (P = 0.07), and 7 s, right side (P = 0.06). The continuous and bursting IES paradigms produced similar levels of pressure reduction around the ITs (1-way ANOVA, P > 0.5).

**IES Increases Signal Intensity in the Atrophied and Loaded Muscles of Human Volunteers with SCI**

MRI images demonstrated that both IES paradigms produced strong contractions and reconfigured muscle shape in all volunteers. A T2*-weighted image of the hip region in one participant is shown (Fig. 5, A and B). IES induced an increase in SI in the gluteal muscles that were loaded and deformed due to sitting, indicating an increase in tissue oxygenation (Fig. 5C). Immediately following both IES paradigms, there was a significant elevation in SI relative to baseline (1-way ANOVA, P < 0.05). The SI remained significantly elevated for the duration of each 10-min scan (1-way ANOVA, P < 0.05) (Fig. 6). The maximal increase in SI produced by the 13-s, 7-s, and bursting protocols averaged across all volunteers was 3.3 ± 0.01%, 2.0 ± 0.01%, and 2.6 ± 0.01%, respectively.
Interestingly, IES resulted in a stepwise increase in SI levels over trials, particularly in individuals whose trials were run consecutively (i.e., without repositioning). In effect, the gains from one trial built on those produced by the previous trial. Examples from two participants (G and I) are shown in Fig. 7. Participant I predicted an oncoming episode of autonomic dysreflexia due to a full bladder following the second IES trial. The disproportionately high SI observed in the third trial likely reflects a systemic increase in oxygen due to activation of the sympathetic nervous system, as well as the increases due to IES. After emptying her bladder, SI returned to a level in line with the rate of increase due to IES.

A slice-by-slice analysis revealed that no spatial differences in SI levels existed relative to the tissue most loaded and deformed by the ITs (data not shown). This suggests that IES induces increases in oxygenation evenly throughout the loaded and deformed gluteus maximus muscles of people with SCI.

IES Increases Signal Intensity in the Loaded Muscles of Anesthetized Rats with Intact Spinal Cords

Similar increases in SI of T₂*-weighted images to those in the human volunteers were seen in the gastrocnemius muscles of rats in response to IES (Fig. 8A). Increases following IES occurred in the stimulated muscle, but not in an adjacent non-stimulated one, suggesting a direct contraction-induced effect on tissue oxygenation. Across rats, the maximal increase in SI relative to baseline after IES was 4.0 ± 0.01%, while the average overall increase was 3.0 ± 0.06% (Fig. 8B).

The comparable increases in SI following IES in loaded tissue between the human and rat models illustrates that the rat model provides a close approximation of IES-induced changes in tissue oxygenation. Undoubtedly, there are differences between the models, including the physiological state and the size of the muscle assessed in each. However, the similarity in the magnitude and pattern of SI increases across the loaded, chronically atrophied muscles in SCI individuals, the loaded, healthy muscles in able-bodied individuals (58, 59), and in the rat model confirms that a general extrapolation between the models is reasonable. Moreover, the increases in SI following IES in the rat model in which rigorous control of position, movement, and sedation was achieved establishes that the increases in SI in the human experiments were not the result of artifacts produced by involuntary contractions or breathing.

IES Produces Substantial Increases in Tissue Oxygen Partial Pressure in Loaded Muscles in a Rat Model

Examples of changes in tissue oxygen partial pressure (PtO₂) produced by IES with different stimulation strengths and levels of muscle loading are shown in Fig. 9A. Immediate increases in PtO₂ were seen following IES, and the oxygenation levels remained above baseline for the duration of the 15-min trials. Cumulative increases in baseline levels of tissue oxygenation similar to the cumulative increases in SI in the SCI volunteers (Fig. 7) were observed in rats. Greater muscle loading reduced the overall increases in IES-induced PtO₂, while changes in IES amplitude (i.e., contraction strength) did not affect the levels of PtO₂. A group summary of the increases in PtO₂ is given in Fig. 9B for two durations of the continuous IES paradigm. Similar to the results seen in humans, the longer “ON” phase duration produced a substantially higher increase in tissue oxygenation. On average, the maximal increases in PtO₂ were 27.7 ± 0.08% and 13.4 ± 0.1% for the 10-s and 5-s “ON” phase durations, respectively. Taken collectively, this suggests that a 4% increase in SI due to IES-induced contractions in loaded and deformed tissue is comparable to a 28% increase in muscle oxygenation.

DISCUSSION

The overall goal of this study was to investigate the effects of IES in counteracting the pathways leading to deep tissue...
breakdown in a population that is highly susceptible to the formation of pressure ulcers. The results demonstrate that IES produces significant reductions in pressure over the ITs and significant, sustained increases in tissue oxygenation. Most importantly, these effects occur in loaded and deformed (due to sitting) atrophied muscles that had not been conditioned before their exposure to IES. The magnitude of the reductions in pressure did not diminish over time, nor did the increases in SI. Furthermore, the stepwise increases in baseline SI and PtO2 (Figs. 7 and 9) indicated that a 1–4% increase in SI occurred per trial. Accordingly, our presentation of the overall average increases in tissue oxygenation due to IES (Fig. 6) is a conservative estimate, because the normalization of SI and PtO2 values to baseline removed the sustained increases between trials.

Interestingly, the results from the present study parallel the effects of IES observed in able-bodied individuals (58, 59). This finding is very compelling given the substantially atrophied muscles of people with SCI, and indicates that the utility of IES is independent of muscle bulk.

Collectively, the results suggest that IES, which consists of short stimulation bouts every few minutes, can provide a dynamic means of relieving pressure and increasing oxygenation throughout the hours of sitting without producing muscle fatigue. This is of importance, as DTI develops from sustained pressure and ischemia. Therefore, IES may be an effective method for preventing DTI in people who have fatigable muscles, such as individuals with SCI.

Comparisons with Previous Work

Pressure-reducing devices and activities, such as static and dynamic pressure-relieving surfaces, repositioning, and wheelchair pushups are regularly prescribed for the prevention of pressure ulcers (19). These approaches allow for periodical redistribution of pressure in passive, noncontracting muscles. IES uniquely allows for active muscle contractions that result in immediate, dynamic pressure reduction in a manner mimicking the constant repositioning and postural readjustments conducted by able-bodied individuals. Moreover, the long-term effects of electrical stimulation can improve muscle
Mechanism of Action of IES

We originally posited that the mechanism underlying the increases in tissue oxygenation by IES was based on changes in blood flow following the induced contractions (i.e., reactive hyperemia or muscle pump action). However, increases in oxygenation due to blood flow occur on the order of seconds (12, 13, 36, 52) and cannot explain the sustained elevations observed in our results. The time course of the initial peak in SI or PtO2 following the 5-, 7-, 10-, or 13-s contractions is similar to that observed in other studies (23) and is attributed to contraction-induced reactive hyperemia (7, 9, 17). Moreover, the magnitude of the transient peak increased with increasing durations of contraction (18, 24).

Nonetheless, the mechanism for the unexpected sustained elevation in tissue oxygenation following the initial peak is currently not fully understood but may be based on the same systems involved in ischemic preconditioning (IPC). In IPC, transient ischemic events push the muscle into a reduced metabolic state, which helps protect against future ischemic events (39, 40, 49). Similarly, the IES-induced contractions may create a transient ischemia, which drives the muscle into a dormant, “protective” state. The decreased oxygen and energy requirements allow the muscle to survive despite the lack of nutrients and energy (27). The reduced need for oxygen would cause a relative increase in the oxygen levels in the microvasculature of the tissue, increasing the SI in T2*-weighted images and PtO2, as observed in the present study.

Conclusions

This work demonstrated that IES effects significant pressure reductions over the ITs, and increases oxygenation in the loaded muscle. The increases in oxygenation were verified by direct, controlled measurements in rats. These results indicate that IES may prevent DTI by directly ameliorating mechanical and vascular pathogenic factors that arise from prolonged tissue loading and deformation. Combined with existing practices, IES may play a substantial role in reducing the incidence of pressure ulcers. A system is currently under development to facilitate the clinical delivery of IES. We envision that IES will be used throughout the hours of sitting or lying down in people with reduced mobility or sensation susceptible to the formation of pressure ulcers.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES


