Enhancing motor learning with a light-weight 3-D Cable-driven Arm Exoskeleton (CAREX)

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Objectives
The CAREX is a novel lightweight upper limb robotic exoskeleton with a cable design which can eliminate gravity and provide path assistance using a force-field. The objectives of this study were to determine the extent of motor learning on a circle drawing task with CAREX in healthy controls and in chronic stroke subjects at earlier and later stages of post-stroke recovery, as defined by their upper extremity Fugl-Meyer (FM) scores.

Design
Seven healthy subjects and nineteen subjects with chronic post stroke right hemiparesis performed 3-sets of 3-D circle drawing using CAREX under 3 randomly assigned conditions: (a) gravity elimination alone, (b) path assistance alone, and (c) path assistance and gravity elimination together. Subjects made a total of 20 circles, 10 clockwise and 10 counter-clockwise, under each of the 3 experimental conditions during a single session.

Results
The path deviation on the circle-drawing task was significantly greater in subjects with stroke across all conditions compared to controls. Subjects were stratified by stage of recovery based on their FM scores into low FM (FM score +3.56) and high FM (FM score >55) (61.6±1.32) subgroups. The high FM subgroup showed least path deviation (0.11±0.04) with path assistance and gravity elimination together comparable to controls (0.08±0.04, p>0.1). In contrast the low FM subgroup showed greatest path deviation under this condition compared with controls (0.26±0.11, p2=-0.53). Control subjects showed no difference in path deviation across the three conditions.

Conclusions
The results suggest that robotic training strategies to control movement trajectory are best provided once sufficient recovery of movement has taken place. Stratification of subjects with stroke based on stage of recovery can determine optimum robotic treatment strategies to improve performance and enhance motor learning post stroke.

Research Study with Best Paper Award Abstract

Objective
Stroke is the leading cause of long-term disability in the United States, and hemiparesis is the most common motor impairment that frequently leads to persistent deficits in hand function. The mechanisms of recovery of hand motor function after stroke are poorly understood and the protocols used in clinical practice lack a solid scientific rationale. A stroke can have profound deleterious effects on functional mobility of the upper limb, and significantly compromise quality of life. Current advances in robotic approaches to stroke rehabilitation provide the opportunity to explore fundamental biomechanical principles that can lead to better strategies to improve upper limb function.

Current designs of exoskeletons using rigid links add inertia to the segments of the human arm making it 4-6 times heavier, which requires subjects to use compensatory non-physiological muscle strategies during movement. Approaches to reducing inertia of the exoskeleton are to place the motors away from the joints and drive the joints using cables and pulleys [e.g. L-exos, CADEN-7, and MEDARM [1-3]]. A novel robotic Cable Driven Upper Arm Exoskeleton, CAREX, consists of 3 lightweight cuffs, one on the shoulder, one on the arm and one on the forearm attached to motor-controlled cables, which makes it 10 times lighter [4] and more versatile than other robotic rehabilitative devices and easy to engage the entire upper limb. In a preliminary study, the CAREX was found to promote near-physiological muscle patterns, similar to those observed during movements without CAREX [5]. Studies have shown that subjects exhibit higher movement accuracy along the desired path with assist-as-needed.
force fields using CAREX [4]. Furthermore, it has been shown that elimination of gravity using partial weight support can reduce abnormal motor synergies in the upper limb after stroke and improve range of motion and function [6, 7]. However, it is not known to what extent path assistance and gravity elimination, which are dissociable using CAREX, contribute to motor learning after stroke, and if patients at different stages of recovery will respond to path assistance and gravity elimination similarly. This is especially important as recent studies suggest that the response to treatment may be diagnostically opposite in patients at different stages of recovery after stroke [8].

In this study we aimed to determine the extent of motor learning on a circle drawing task with CAREX under three experimental conditions – gravity elimination alone, path assistance and gravity elimination and path assistance alone in healthy controls and in chronic stroke subjects at earlier and later stages of post-stroke recovery as defined by their total upper extremity Fugl-Meyer (FM) scores (max score = 66).

**Design**
Seven healthy subjects and nineteen subjects with chronic post stroke right hemiparesis performed 3-sets of 3-D circle drawing using CAREX under 3 randomly assigned conditions: (a) gravity elimination alone, (b) path assistance alone, and (c) path assistance and gravity elimination together. While seated with the torso secured with a four-point seat belt, subjects followed a prescribed circular path with a constant diameter of 15 cm formed by 2 rods clamped on an adjacent stand providing 3 points through which to draw a 3-D circle. Subjects made a total of 20 circles, 10 clockwise and 10 counter-clockwise, under each of the 3 experimental conditions during a single session. The conditions were counterbalanced to reduce order effects. Rest breaks were given to reduce fatigue. Subject performance on the Fugl-Meyer Scale was logged at baseline and kinematic data were recorded by the potentiometers within the CAREX.

**Results**
The path deviation on the circle-drawing task, as calculated by the mean normalized distance from target trajectory, was significantly greater in subjects with stroke across all conditions compared to controls. Subjects were stratified by stage of recovery based on their FM scores into low FM (FM score +3.56) and high FM (FM score >55) (61.6±1.32) subgroups. The high FM subgroup showed least path deviation (0.11±0.04) with path assistance and gravity elimination together comparable to controls (0.08±0.04, p>0.1). In contrast the low FM subgroup showed greatest path deviation under this condition compared with controls (0.26±0.11, p<0.4). The FM scores were inversely related to path deviation with path assistance provided with the CAREX ($r^2$=-0.53). Control subjects showed no difference in path deviation across the three conditions.

**Conclusion**
Motor training using the novel, light weight CAREX robotic device was well tolerated by subjects with chronic stroke with a wide range of FM scores. However, individuals at different stages of post-stroke motor recovery, as defined by their FM scores, responded differently to training under various conditions with the robot. Path assistance was detrimental to learning in subjects at an earlier stage of recovery but helpful in subjects at a later stage of recovery suggesting that strategies to control movement trajectory are best provided once sufficient recovery of movement has taken place. Stratification of subjects with stroke based on their stage of recovery can determine optimum robotic treatment strategies to improve performance and potentially enhance motor learning for functional restoration post stroke.
Combined cerebral and spinal non-invasive direct current stimulation on upper limb recovery in chronic iSCI: A Case Series

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Objectives
The objective of this study is to evaluate the effects of non-invasive anodal transcranial direct current stimulation (tDCS) and non-invasive anodal transcutaneous spinal direct current stimulation (tsDCS) combined with robotic-assisted training (R-A training) on upper limb motor function in adults with chronic tetraplegia due to incomplete spinal cord injury (iSCI). The literature and preliminary data suggest that non-invasive brain and spinal cord stimulation with R-A training will significantly increase arm and hand function compared to treatment with combined brain stimulation and R-A training.

Design
This study uses a matched case-control design. Four adults with chronic, cervical iSCI (AIS C and D levels) are assigned to receive either tDCS and tsDCS combined with R-A training or tDCS combined with R-A training. Treatment is administered five sessions per week for two weeks. Assessment of upper extremity motor behavior for the training arm is performed at baseline and at the end of ten sessions. The primary clinical measurement for motor behavior is the Jebsen-Taylor Hand Function Test (JTHFT). The ASIA Upper Extremity Scale for motor and sensory assessment, the Modified Ashworth Scale (MAS), and grip and pinch strength are secondary clinical measurements.

Results
Two subjects have been enrolled in the study and are undergoing treatment. Subject 1 is a 59 year-old male with a history of traumatic, C3-C4 ASIA D SCI. Time since injury is 84 months. Subject 2 is a 64 year-old male with a history of traumatic, C3-C6 ASIA D SCI. Time since injury is 60 months. Baseline assessment of upper extremity motor and sensory behavior in the training arm has been measured for both subjects.

Conclusions
This study is ongoing. Data will continue to be collected in order to verify whether non-invasive brain stimulation combined with non-invasive spinal cord stimulation and R-A training will improve upper-limb motor function compared to brain stimulation and R-A training.

Research Study with Best Paper Award Abstract

Background: Impairment of arm and hand function due to spinal cord injury (SCI) reduces independence in daily living activities such as self-care (e.g., feeding, bathing, dressing, toileting), social activities, and work. Improvements in upper-extremity strength in persons with tetraplegia can make a clinically significant difference in quality of life.

Transcranial direct current stimulation (tDCS) and transcutaneous spinal cord direct current stimulation (tsDCS) are safe, non-invasive brain and spinal cord stimulation techniques which use constant, weak direct current delivered across the scalp and neck to target brain and spinal cord regions via small electrodes. tDCS has been used to modulate activity of the cerebral cortex by inducing marked changes in cortical excitability. Brain polarization promotes lasting synaptic changes via long-term potentiation (LTP) and depression (LTD), as well as non-synaptic mechanisms. Recently, the use of direct currents on the brain has been implemented into transcutaneous direct current stimulation to modulate spinal cord function. Given that the brain and spinal cord interact through several projections such as corticospinal pathways, stimulation over the spine may modulate different supraspinal activities and hence makes tsDCS a desirable tool for clinical applications.
The literature and preliminary data support the model that augmentation of activity in spared corticospinal tract (CST) axons is a critical mechanism of motor improvement, and furthermore that CST activity can be increased by repetitive motor training of single joint movements and by electrical stimulation of the primary motor cortex (M1). Therefore, the purpose of this study is to evaluate if adults with chronic tetraplegia caused by incomplete spinal cord injury (iSCI) can improve their upper-limb voluntary movement by participating in a therapeutic program that combines non-invasive brain and spine stimulation with robotic-assisted training (R-A training). We hypothesize that subjects who receive ten sessions of anodal tDCS combined with anodal tsDSC and R-A training over two consecutive weeks will exhibit greater improvement in arm and hand functions compared to anodal tDCS and R-A training.

**Methods:** This study uses a matched case-control design. Four adult participants with motor incomplete spinal cord injury (AIS levels C and D) are recruited from TIRR Memorial Hermann and the Houston area. Subjects are included if they have: (1) diagnosis of chronic incomplete cervical lesion as defined by the American Spinal Injury Association Impairment scale classification; (2) upper-extremity weakness associated with tetraplegia; (3) age at least 18 years; (4) no brain injury; (5) no planned alteration in upper-extremity therapy or medication for muscle tone during the course of the study; (6) no contradiction to tDCS. Subjects are excluded if they have: (1) prior history of seizure; (2) chronic use of neuroactive medication; (3) a Modified Ashworth Score > 3 out of 4.

Subjects in the experimental group receive anodal tDCS (2 mA) for 20 minutes on the motor cortex contralateral to their trained side, followed by anodal tsDCS (2.5 mA) on C3-C5 unilateral to their trained arm for 15 minutes, and R-A training for 60 minutes. Participants in the control group receive 2 mA anodal tDCS for 20 minutes and sham tsDCS, followed by R-A training for 60 minutes. Treatment will be administered at an intensity of five sessions per week for two weeks.

Assessment of upper extremity motor behavior for the training arm is performed at baseline and at the end of ten sessions. The primary clinical measurement for motor behavior is the Jebsen-Taylor Hand Function Test (JTHFT). The ASIA Upper Extremity Scale for motor and sensory assessment, the Modified Ashworth Scale (MAS), and grip and pinch strength are secondary clinical measurements.

**Results:** Two subjects have been enrolled in the study and are undergoing treatment. Baseline assessment of upper extremity motor and sensory behavior in the training arm has been measured for both subjects.

Subject 1 is a 59 year-old male with a history of traumatic, C3-C4 ASIA D SCI. Time since injury is 84 months. This subject also has a history of arthritis and hypercholesterolemia. Subject 1 has a baseline ASIA Upper Extremity Motor Score of 18, an ASIA light touch sensory score of 56, and an ASIA pinprick sensory score of 56. Subject 1 has a grip strength of 10.2 kg and pinch strength is 8.6 kg. The participant has a baseline JTHFT page turning time of 10.1 seconds, lifting time of 19.2 seconds for small common objects, stimulated feeding time of 9.4 seconds, stacking checkers time of 14.8 seconds, lifting time of 7.2 seconds for large and light objects, and lifting time of 7.3 seconds for large and heavy objects. The total JTHFT score for the trained arm in subject 1 was 68.6 seconds for 30 items.

Subject 2 is a 64 year-old male with a history of traumatic, ASIA D SCI at levels C3-C6. Time since injury is 60 months. Subject 2 has a baseline ASIA Upper Extremity Motor score of 18, an ASIA light touch sensory score of 39, and an ASIA pinprick sensory score of 31. This subject has a grip strength of 5.3 kg and pinch strength of 3.6 kg in the trained arm. The subject has a JTHFT page turning time of 13.5 seconds, lifting time of 32.8 seconds for small common objects, stimulated feeding time of 22.9 seconds, stacking checkers time of 19.5 seconds, lifting time of 11.3 seconds for large and light objects, and lifting time of 13.4 seconds for large and heavy objects. The total JTHFT score for the trained arm in subject 2 was 113.5 seconds for 30 items.

**Conclusion:** This study is ongoing. Data will continue to collected in order to verify whether non-invasive brain stimulation combined with non-invasive spinal cord stimulation and R-A training will improve upper-limb motor function compared to brain stimulation and R-A training.
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Impact of distraction on brain computer interface control of a robotic arm during a motor task

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Objectives
Our goal was to examine how distractions affect the performance of a brain-computer-interface (BCI) driven prosthetic arm and whether any neural correlates of distraction could be observed. We hypothesized that with increasing distraction, there would be a decrease in performance and an increase in neural firing rate.

Design
The subject had two intracortical microelectrode arrays (MEA) implanted in her primary motor cortex. Firing rates were transformed into two-dimensional endpoint velocity command signals for a robotic arm. The subject was instructed to move the arm between two targets as many times as possible during a 60 second trial. The following distraction variables were introduced: background noise, counting and subtracting, counting backwards by 3, using a chin joystick, and answering questions. The subject’s performance (number of targets/minute), perceived difficulty rating, and neural and kinematic data were recorded.

Results
The number of targets hit, as well as, the subject’s perceived difficulty rating did not show a statistically significant difference between distraction variables. The subject reported the joystick operation distraction variable as the most difficult overall, although this rating was not statistically significant over other variables when compared across days. A significant decrease in firing rate was observed while the subject counted backwards by 3 during the motor task. (p < 0.005) Without motor task, a decrease in firing rate was observed during background noise, counting and subtracting, and moving the chin joystick, compared to baseline (p < .005).

Conclusions
Counter to our hypotheses, no changes in performance were observed, and the only changes in neural firing showed a decrease during distraction. It is possible that the distractions were not difficult enough to impact performance on a fairly simple BCI task. In some cases, the subject may have been more relaxed during the distraction. Overall, this is encouraging, as it appears that BCI control is robust to these types of distractions.

Research Study with Best Paper Award Abstract

Background: Brain-computer interface (BCI) controlled prosthetics show promise for dramatically improving the lives of patients who are severely disabled. A BCI can decode neural firing patterns into useful command signals for prosthetics, which could restore some of the independence lost after a patient experiences severe paralysis. A robust and useful BCI would need to be usable even when other prominent stimuli are present. Environmental stimuli could include distractions or the act of multi-tasking such as operating a BCI while holding a conversation. Previous data in our lab has observed an increase in firing rate as the subject approaches an object as compared to free reaching, which we hypothesize is because object interaction requires more mental effort. Similar data from monkeys shows a decrease in neural firing rate when the monkey is not attending to a task. From this data, we deduced that as attention increases, so does firing rate. Since firing rate is transformed into command signals for the robotic arm, it must be accounted for properly by the BCI, or changes in firing rate will impact performance. To test this, we examined a subject’s ability to perform a simple motor task with a robotic arm controlled by her BCI while several different distraction stimuli were introduced. Our first hypothesis was that increased distraction
would result in decreased performance, as measured by number of targets hit during each trial. It was reasoned that as the subject’s cognitive load increased due to distraction, her ability to maintain fidelity of the firing patterns required for control of the robotic arm would be reduced. Our second hypothesis was that with increased distraction there would be an increase in neural firing rate as cognitive load increases with heightened efforts to maintain attention on the task.

Design: The subject had two intracortical microelectrode arrays (MEA) implanted in her primary motor cortex. Firing rates were collected and processed by a decoder that transformed them into two-dimensional endpoint velocity command signals for control of a robotic arm. The subject was instructed to move the arm between two targets as many times as possible during a 60 second trial. A hit was registered when the hand tapped a physical target on either end of the experimental space. During some of the trials the following distraction variables were introduced: background noise, counting two sets of auditory tones and mentally subtracting the smaller from the larger, counting backwards from a random number by 3, using a chin joystick to move a cursor to a specified point, and answering conversational questions. The subject’s performance (targets hit/minute), perceived difficulty rating, and neural and kinematic data were recorded. These trials were then compared to a baseline, which consisted of the same data collected during the motor task with no distraction variable. Data was also collected for each distraction variable while the subject was at rest, i.e. not performing the motor task, and this was compared to a baseline with no distraction stimuli. Each condition was repeated twice on 5 days of testing and combined into a single data set.

Statistical analysis: Average firing rates during distractions were compared to baseline using a Wilcoxon sign rank test for data sets collected during motor BCI performance. The same test was applied to the data collected during the distractions without the motor task, which were compared to recordings taken while the subject was at rest. A Bonferroni corrected p < 0.005 was used to assess significance. The number of targets acquired during distraction was compared to performance with no distraction using a t-test.

Results: Both the number of target hits, as well as the subject’s perceived difficulty rating of each distraction variable, failed to show a statistically significant difference between distraction variables. The subject reported chin joystick operation as the most difficult overall with a rating of 4.2 (on a 10 point scale where 1=very easy and 10=very difficult) although this rating was not statistically significant over other the other conditions (difficulty ranged from 3.4-4.1). A significant decrease in firing rate compared to baseline was observed while the subject counted backwards by 3 during the motor task. (p < 0.005) Additionally, when not using the BCI to perform the motor task, a decrease in firing rate was observed during background noise, counting and subtracting, and moving the chin joystick, compared to baseline (p < 0.005).

Conclusions: Counter to our hypotheses, no changes in performance were observed, and the only significant changes in neural firing showed a decrease during distraction. It is possible that the distractions were not difficult enough to impact performance on simple BCI motor tasks. In some cases, the subject may have been more relaxed during the distraction, as the “distraction condition,” such as conversation, might have actually served to lessen the strain of trying too hard at the task. Additionally, the choice of a repetitive motor task, as opposed to a varied one, might have allowed the subject to slip into a reflexive motor pattern, thus not impacting the subject’s performance. The choice of distraction variable could have also played a role in how the distraction impacted neural firing patterns in the primary motor cortex. That is, the count and subtract variable would access very different regions of the brain than the joystick control task, and different still from the conversation task. In future explorations on distraction in BCI, one should consider the affected areas of cortex compared to the location of the BCI recordings, and also vary the difficulty of distraction over a larger range. Overall, it is encouraging that BCI performance was not impacted during these distraction tasks as it appears that microelectrode-based BCI performance is robust to this level of distraction.

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Determinants of recovery from a 161-km ultramarathon

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Objectives
This study examined short-term recovery from a 161-km ultramarathon through functional and subjective measures, and explored which factors determined the rate of recovery.

Design
Participants of the 2015 161-km Western States Endurance Run completed two 400 m runs at maximum speed during the 21 days before the race and on days 3 and 5 after the race, underwent a blood draw for plasma creatine kinase (CK) concentration post-race, and provided lower body muscle pain and soreness ratings (10-point scale) and overall muscular fatigue scores before the race, immediately after the race and for the subsequent 7 days.

Results
Among the 72 race finishers completing the study, 400 m run times were 26.3% slower (p=0.001) at day 3 and 12.4% slower (p=0.01) at day 5 compared with pre-race times. Muscle pain and soreness ratings and muscular fatigue scores had statistically returned to pre-race levels by 5 days post-race. Lower body muscle pain and soreness across the recovery period was modeled by time (decreased by 1.1 points each day), post-race plasma CK concentration (0.8 and 1.5 points higher for CK value of 10,001-27,999 and ≥28,000 U/L compared with ≤10,000 U/L, respectively), and age (0.4 points lower for each decade of aging).

Conclusions
Post-race plasma CK and age are the main determinants of resolution of lower body muscle pain and soreness following an ultramarathon. Appropriate training would be recommended to attenuate muscle damage and optimize ultramarathon recovery.

Research Study with Best Paper Award Abstract

INTRODUCTION
Ultramarathons are longer than traditional 42-km marathons and often take place on tracks, roads and in the wilderness. The physiological stress from running extended distances may be compounded by challenging terrain and adverse environmental conditions. Participation has grown exponentially and an increasing number of individuals are running multiple ultramarathons each year. As such, an understanding of factors that enhance recovery is important.

The purpose of this study was to examine short-term recovery from a 161-km ultramarathon through functional and subjective measures, and explore which factors determine recovery. We also examine whether an objective measure of muscle damage (plasma creatinine kinase (CK) concentration) is predicted by subjective and functional measures shortly after the race.

METHODS
The study was performed at the 2015 Western States Endurance Run, a 161-km single-track ultramarathon through the Sierra Nevada Mountains of northern California with cumulative ascent of 5500 m and descent of 7000 m. Subjects were recruited electronically. The VA Northern California Health Care System provided IRB approval.

Lower body muscle pain and soreness (10-point Likert scale) and overall muscular fatigue (12-cm visual analog scale) ratings were obtained at registration, immediately after finishing, and the subsequent seven mornings after being up and moving around for approximately 30 minutes. Immediately after the race, a blood sample was drawn from seated runners into a heparinized tube for plasma creatine kinase (CK) concentration.
A 400 m run at maximal speed was performed twice on separate days during the 21 days before the race and on the third and fifth days after the race.

Linear mixed models with repeated measures was used to assess variables associated with post-race lower body muscle pain and soreness. Time was the repeated measures factor and included measurements immediately post-race and post-race days 1 through 5. Fixed effects considered included age, sex, post-race plasma CK concentrations, race finish time, difference between predicted and actual finish time, pre-race 400 meter run time, number of years of regular running, number of years of running ultramarathons, number of 161-km ultramarathons completed, number of 161-km ultramarathons started, average weekly running distance, highest week running distance and longest training run or race during the prior 3 months.

RESULTS
There were 388 race entries, 107 study enrollees and 98 starters who completed the pre-race requirements. Of the starters, 73 finished the race and 72 completed the post-race intervention and data collection.

All recovery variables showed a significant time effect (p < 0.0001). The lower body muscle pain and soreness rating and overall muscular fatigue score statistically returned to baseline after 5 days. Compared with the second pre-race 400 m run, times were 26.3% slower (p=0.001) at day 3 and 12.4% slower (p=0.01) at day 5.

Time (F (1, 363.21) = 500.03, plasma CK concentration (F (2, 85.21) = 9.94, p < 0.001), and age (F (1, 85.20) = 7.821, p < 0.007) were found to model muscle pain and soreness during the 5 days following the race. Post-race muscle pain and soreness decreased 1.1 points each day and 0.4 points with each decade of increasing age. Runners with the highest post-race CK concentrations had ratings 0.8 points higher than runners with the lowest CK concentrations. Younger runners and those with high CK concentrations reported the highest ratings, but ratings decreased at the same rate for all runners.

Plasma CK concentrations was directly associated with lower body muscle pain and soreness immediately post-race and at day 1 post-race, overall muscular fatigue at day 1 post-race, and relative change in 400 m run time at day 3 compared with pre-race.

Discussion
Post-race CK concentrations and age were the main determinants of lower body muscle pain and soreness following an ultramarathon. Higher CK concentrations were associated with greater ratings and older age with lower ratings. The findings suggest that attenuating the extent of muscle damage, evidenced by CK, may optimize recovery and can be achieved through training.

Lower body muscle pain and soreness rating, and overall muscular fatigue score, were at their highest immediately post-race before returning to baseline within 1 week (day 5 statistically). Past studies at 161- to 166-km ultramarathons have similarly shown peak values immediately post-race with return to baseline within 5-9 days. Given the race duration and resulting muscular damage, it is not surprising that there is a leftward shift of the classical post-exercise muscle pain profile in which pain peaks at 24-72 hours.

Although post-race CK was statistically related to muscle pain and soreness immediately and day 1 post-race, the fatigue on post-race day 1, and the change in 400 m run time at day 3 post-race compared with pre-race, the subjective and functional measures accounted for only 6-16% of the variability in post-race CK concentrations. Therefore, these measures are not good surrogates for the extent of rhabdomyolysis.

CONCLUSION
This study showed that time, age, and plasma CK concentrations were significant determinants of lower body muscle pain and soreness following a 161-km ultramarathon. Post-race muscle pain and soreness ratings were
higher in runners who were younger and had higher plasma CK concentrations. Given that training attenuates muscle damage, it would follow that appropriate training is the optimal approach to enhance ultramarathon recovery.

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Association Between Time-to-Rehabilitation and Outcomes Following Traumatic Spinal Cord Injury

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Objectives
The benefits of earlier rehabilitation following traumatic spinal cord injury (SCI) remain uncertain. The objective of this study was to examine the relationship between time-to-rehabilitation (TTR) following SCI and rehabilitation outcomes, as measured at discharge and 1-year post injury.

Design
We conducted a retrospective study using data from 23 Spinal Cord Injury Model Systems across the United States. Patients experiencing a traumatic SCI between 2000 and 2014, who were 18 years or older, and who were admitted to a Model System within 24 hours of injury, comprised our study population (N = 3,937). TTR was measured as the number of days between injury and admission to inpatient rehabilitation. Pre-specified outcome measures included the Functional Independence Measure (FIM) motor score at discharge and 1-year post injury (Rasch-transformed), a dichotomous measure of discharge to a private residence, and the Craig Handicap Assessment and Reporting Technique (CHART) Physical Independence and Mobility scores (scaled 0-100) at 1-year post injury. Instrumental variables regression was used to reduce confounding from unobserved severity of illness/comorbidities. All models controlled for sociodemographic and injury characteristics (including injury severity), FIM motor score at admission, and rehabilitation length of stay.

Results
After adjusting for health status, a 10% increase in TTR was associated with a 1.50 lower FIM motor score at discharge (95% CI, -2.43 to -0.58; P=0.001) and a 3.92 lower CHART Physical Independence score at 1-year post injury (95% CI, -7.66 to -0.19; P=0.04). Compared to the mean FIM motor score (37.5) and CHART Physical Independence score (74.7), these represent relative declines of 4.0% and 5.3%, respectively. There was no association between longer TTR and the likelihood of discharge to a private residence, 1-year FIM motor score, or the CHART mobility score.

Conclusions
Efforts to promote earlier rehabilitation following traumatic SCI may improve patients’ functional status at discharge.

Research Study with Best Paper Award Abstract

OBJECTIVE
Background and Purpose: Approximately 12,000 Americans experience traumatic spinal cord injury (SCI) each year, the incidence of which has remained stable over the past decades. During the same period, both acute care and rehabilitation lengths of stay (LOS) for SCI have fallen markedly. Despite this, the duration of time that patients with SCI spend in an acute care setting still varies widely, and this variation may or may not be related to patients’ underlying severity of illness and medical need. Delays in transferring to rehabilitation often occur during a time when harnessing neuroplasticity is crucial for functional recovery. Additional days spent in acute care while
forgoing rehabilitation may provide little or marginal benefit.

Limited past research has suggested that earlier rehabilitation may improve functional status for patients with SCI. However, these studies (over 10 years old, with small numbers of patients in Italy and Japan) may not generalize to the United States. Thus it remains unclear whether differences in the time from injury to rehabilitation impacts patient outcomes. The objective of this study was to examine the relationship between time-to-rehabilitation (TTR) following SCI and rehabilitation outcomes at discharge and 1-year post injury. We hypothesized that longer TTR would be negatively associated with outcomes.

DESIGN
Data Source: Data were obtained from the Spinal Cord Injury Model Systems (SCIMS), a network of federally funded facilities that has collected data on demographic and clinical characteristics for approximately 13% of all SCI cases in the United States since 1973.

Subjects: Patients experiencing traumatic SCI between 2000 and 2014 (N = 10,506), who were at least 18 years of age at the time of injury (N= 9,969) and were admitted to a Model System facility within 24 hours of injury (N= 4,256) were included. The final study population consisted of 3,937 patients treated in 23 Model Systems.

Measures: TTR, the main exposure, was measured as the number of days between the injury and admission to inpatient rehabilitation. Pre-specified outcome measures were selected on the basis of prior research and the plausibility that they would be impacted by differences in TTR; these included the Functional Independence Measure (FIM) motor score at discharge and 1-year post injury (Rasch-transformed), a dichotomous measure of discharge to a private residence, and the Craig Handicap Assessment and Reporting Technique (CHART) Physical Independence and Mobility subscale scores (scaled 0-100) at 1-year post injury.

Statistical Analysis: The fundamental challenge of determining if TTR influences outcomes is confounding by unobserved severity of illness and comorbidities—more severely ill patients likely require longer acute care stays prior to transfer to rehabilitation. As such, their total TTR will be longer and they could be more likely to have poorer functional statuses and outcomes. Consequently, earlier rehabilitation will appear beneficial in standard regression analyses—a result that may be biased by unobserved confounders. We used instrumental variables regression to attenuate confounding from both observed and unobserved confounders. Use of this technique requires identifying an observable variable (the “instrument”) that is strongly correlated with TTR (instrument relevance) but is uncorrelated with severity of illness and has no direct effect on rehabilitation outcomes (instrument validity).

Because traumatic SCI represents an exogenous, unexpected, and acute change in health status, there is little reason to believe that the geographic location where the injury occurs is related to patients’ severity of illness, but it is related to provider practice patterns concerning LOS. We therefore exploit geographic variation in the intensity of inpatient days utilized for terminally ill Medicare beneficiaries in each Model System’s hospital referral region as an instrumental variable. This measure, collected by The Dartmouth Atlas of Health Care, reflects a region’s tendency toward utilizing additional days of care (relevance) for patients who have similar health statuses because they are all terminally ill (validity). Such end-of-life measures have been used previously as instrumental variables. All models controlled for sociodemographic and injury characteristics (including neurologic level and completeness of injury), FIM motor score at admission to rehabilitation, and inpatient rehabilitation LOS (to control for the independent effect of rehabilitation).

RESULTS
The average age of patients at injury was 41.5 years old; 79.2% were male, 62.8% white, and 16.6% had C1-4 injuries with an American Spinal Injury Association Impairment Scale of A, B, or C. The average TTR was 19.0 days (SD, 23.0). A 1-day increase in region-level average inpatient days among terminally ill Medicare beneficiaries (the instrumental variable) was associated with a 9% increase (95% CI, 6% to 13%) in TTR among patients in our study population, demonstrating instrument relevance. In the instrumental variable analyses that adjust for health
status, a 10% greater TTR was associated with a 1.50 lower FIM motor score at discharge (95% CI, -2.43 to -0.58; P=0.001) and a 3.92 lower CHART Physical Independence score at 1-year post injury (95% CI, -7.66 to -0.19; P=0.04). Compared to the mean FIM motor score at discharge (37.5) and CHART Physical Independence score (74.7), these represent relative declines of 4.0% and 5.3%, respectively. There was no association between longer TTR and the likelihood of discharge to a private residence, 1-year FIM motor score, or the CHART mobility score.

Limitations: Because the SCIMS data are restricted to a small set of facilities, we confronted limited region-year variation in our instrumental variable. Nevertheless, our sensitivity analyses that included alternative instrumental variables were consistent with our main results and supported the validity of the instrumental variable approach. Additionally, it is unclear whether our results would generalize to patients with SCI treated in non-SCIMS facilities, though prior research has demonstrated that SCIMS data are broadly representative of the population of patients who experience traumatic SCI in the United States.

**CONCLUSIONS**
Using a national sample of data on SCI patients spanning 15 years, our results complement and extend existing research on traumatic SCI that has demonstrated functional benefits to earlier rehabilitation. Efforts to promote earlier rehabilitation following traumatic SCI, through quality improvement interventions or enhanced collaboration between acute and post-acute care providers, may improve patients’ functional status at discharge.

### Variations in Rehabilitation Regimens and their Impact on Treatment Outcomes for Rotator Cuff Tears

**Author(s)**
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**Objectives**
Patients with rotator cuff tears are commonly referred for non-operative treatment. There is a lack of data on use of physical therapy techniques, compliance with programs, and home-based therapies. Our objective was to assess variations in rehabilitation programs and their impact on outcomes for degenerative rotator cuff tears.

**Design**
Subjects: Patients with rotator cuff tears confirmed on clinical examination and imaging. Methods: Our ongoing longitudinal cohort study includes data from 108 patients undergoing non-operative treatment for rotator cuff tears. All patients were prescribed physical therapy and were considered compliant if they reported performing exercises by six-month follow-up. Each participant completed questionnaires at enrollment, and 3, 6, and 12 months of follow-up. The Shoulder Pain and Disability Index (SPADI) was our primary outcome measure.

**Results**
Mean SPADI scores showed significant improvement by final follow-up (45.6 +/-24.4 to 25.3 +/-22.8), with pain subscores decreasing at a higher rate than disability scores. The compliance rate with physical therapy was 88.6%. There were similar patterns of decrease in SPADI for patients doing physical therapy with a therapist versus those performing exercises at home only. The most commonly used techniques were stretching (46%), strengthening (45%), bands (32%), and weights (33%). Patients performing strengthening or stretching exercises had better outcomes by 6 months than those not performing strengthening or stretching.

**Conclusions**
Physical therapy can result in significant clinical improvement for patients with degenerative rotator cuff tears. Patients undergoing rehabilitation with a physical therapist had similar outcomes as compared with those performing exercises only at home. Patients who incorporated stretching or strengthening into their rehabilitation program had better pain and function as compared with patients who were not stretching or strengthening. This data can be used to design a standardized evidence-based rehabilitation program for non-operative treatment of rotator cuff tears.
Research Study with Best Paper Award Abstract

Objectives:
Shoulder pain accounted for 11.5 million ambulatory care visits to physician offices in 2010 in the United States. Most patients with cuff tears are treated non-operatively and prescribed a rehabilitation program, which is estimated to be successful 42% to 82% of the time. Effectiveness likely depends on components of the rehabilitation program, such as strengthening of the rotator cuff, stretching of the capsule, and scapular stabilization. Several modalities such as acupuncture, transcutaneous electrical nerve stimulation (TENS), and ultrasound are also available. However, data on components of physical therapy programs and their effect on outcomes is lacking. The objective of this study was to understand variations in physical rehabilitation programs and their effect on treatment outcomes for non-operative treatment of rotator cuff tears. We also examined treatment compliance and at-home versus clinic-based programs.

Design:
We enrolled 180 patients in an ongoing, multicenter cohort study. Patients over 45 years old with shoulder pain lasting at least 4 weeks were included and enrolled if a cuff tear was found on clinical exam and MRI review. Exclusion criteria were prior fracture or surgery of the index shoulder. Patients were referred for operative or non-operative treatment by their attending physician. Each participant completed a baseline questionnaire, and was followed at 3, 6, and 12 months. If patients did not return the questionnaire, up to three follow-up phone calls were made to reach them. Independent research assistants entered data into two databases, which were subsequently compared. Discrepancies were resolved by examining the patients’ original questionnaires.

Of the 180 enrolled patients, 108 patients were prescribed physical therapy. Patients were considered compliant if they reported performing exercises (at home or with a therapist) on their three or six month follow-up questionnaires. We elicited information on use of stretching, strengthening, bands, weights, ultrasound, ultrasound with topical corticosteroid, and electrical stimulation. Our primary outcome measure was the Shoulder Pain and Disability Index (SPADI), a validated questionnaire that assesses ability to perform activities of daily living through pain and disability subscales. We analyzed SPADI over time to determine the extent to which compliance with treatment, at-home therapy versus clinic-based therapy, and the aforementioned aspects of the therapy program were associated with changes in outcome.

Results:
Of the 108 enrolled patients, 99 patients had available SPADI data at baseline, 59 at 3 months, 51 at 6 months, and 51 at 12 months (some patients had not yet reached their follow-up time points). SPADI scores decreased significantly from a mean of 45.6 +/-24.4 at baseline to 25.3 +/-22.8 by final follow-up. This exceeds the minimal clinically important difference for change in SPADI (8 points). While disability scores were lower than pain at baseline (36.1 +/-23.9 versus 45.6 +/-24.4), they improved at a slower rate than pain over the course of treatment. Between 3 months and 6 months, disability scores improved only 0.5 points on average.

Only 8 patients did not comply with the prescribed physical therapy. While the sample size was small, the noncompliant group was found to have a mean baseline SPADI score 10.5 points lower (less pain and disability) than those who were compliant with therapy (p=0.2 for difference between the compliant and non-compliant groups). SPADI scores for the compliant group decreased 16.9 points (42.7 +/-23 at baseline to 25.8 +/-22.6 at 12 months), exceeding the minimal clinically important difference. The noncompliant group saw a change of only 6.5 points over 12 months (32.2 +/-17.1 to 25.7 +/-26.1).

At 1-year follow-up, 75% of patients were still performing exercises. Of these, 35% were still seeing a physical therapist. There were similar patterns of decrease in SPADI for patients doing physical therapy and home therapy versus those performing exercises only at home (p=0.7 for difference in the two groups).

In our cohort, 46% of patients were stretching, 48% were strengthening, 32% were using bands, and 33% were using weights in their rehabilitation program. Only 6% reported using ultrasound, 2% using ultrasound with
corticosteroid, and 9% using electrical stimulation. The most frequent combinations of techniques were stretching and strengthening (7%), and stretching and strengthening with bands and weights (11.5%). We found the mean SPADI score of patients reporting stretching in their rehabilitation program was 29.7 +/-24 at 3 months compared to 40.1 +/-21 for those not stretching (p=0.17). Similarly at 6 months, mean scores were 22.6 +/-19.6 for stretching compared to 36.5 +/-19.6. We saw similar trends for patients undergoing strengthening. Compared to those not strengthening, mean SPADI scores were 31.3 +/-23.6 versus 39.7 +/-25.8 at 3 months, and 26.5 +/-20.28 versus 33 +/-26.5 at 6 months.

Conclusions: There were significant improvements in treatment outcomes of patients with rotator cuff tears undergoing rehabilitation at 1 year of follow-up. Pain scores decreased to a greater extent than disability scores. This may imply that factors in addition to pain are associated with functional disability in patients with rotator cuff tears. Patients undergoing rehabilitation with a physical therapist had similar outcomes as compared with those performing exercises only at home. The most common rehabilitation techniques were stretching, strengthening, bands, and weights. Patients who incorporated stretching or strengthening into their rehabilitation program had better pain and function as compared with patients who were not stretching or strengthening. Thus, our study provides data on rehabilitation program components and their association with outcomes in patients with rotator cuff tears. This data needs to be replicated in larger studies and can be used to design a standardized evidence-based rehabilitation programs for non-operative treatment of rotator cuff tears.

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The hip-spine connection: physical examination findings in adolescent and young adults with low back pain

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Objectives
The objective is to describe hip physical examination findings in adolescents and young adults presenting for evaluation of low back pain (LBP) and compare pain and function in those with findings of both a hip and spine disorder to those with findings of a spine disorder alone.

Design
This is a prospective observational cohort study of consecutive patients (ages 10-23) presenting for evaluation to a physiatrist for evaluation of LBP. Validated patient reported pain, hip and lumbar spine functional questionnaires were obtained including: pain diagram, numeric pain rating (NPR), modified Oswestry Index (mODI), Rolland-Morris (RMQ), UCLA activity score, modified Harris Hip Score (mHHS), STarT Back Screening Tool, and HOOS Hip Survey. A musculoskeletal and neurological examination was performed by a single examiner and results were recorded. Specific hip tests including goniometer measurement of hip range of motion and hip provocative tests were performed. Patient characteristics, pain and function were compared between those with and without positive hip findings.

Results
24 consecutive patients (18 women, 6 men) with a mean age of 18.9 years (SD±3 years) and mean BMI of 23.7 kg/m2 (SD±5 kg/m2 ) were enrolled. On physical examination 1) 3 (12.5%) displayed an antalgic gait, 2) 13 (54%)
had < 20° of hip internal rotation and 3) 5 (20%) had 1, 6 (24%) had 2 and 10 (40%) had 3 positive provocative hip tests. Those with < 20° of hip internal rotation were found to have worse (p=.02) hip functional scores as measured by mHSS.

Conclusions
This is the first data to describe connections between hip and spine in adolescent and young adult populations presenting with LBP. Further study is needed to define how hip disorders impact and contributes to LBP.

Acknowledgements:
This study was funded by the Rehabilitation Research Experience for Medical Students (RREMS) Program.

Research Study with Best Paper Award Abstract
Objectives: Describe lumbar spine and hip physical examination findings in young adults and adolescents presenting for evaluation of low back pain (LBP) and compare pain and function of people with hip and spine findings as compared to those with spine findings alone.

Background: Etiologies of LBP are poorly understood. Literature regarding co-existing hip and spine disorders describes a hip-spine syndrome associated with pain and disability. Impact of coexistent conditions on disease progression and treatment response is unknown. All descriptions have focused on adult populations, primarily with hip and/or spine arthritis. No studies have shown these connections in a population that may be experiencing LBP for the first time or early in their course. Describing prevalence of physical examination findings of a hip disorder in adolescents and young adults presenting for evaluation of LBP and comparing pain and function in those with and without physical examination findings of a hip disorder will provide data to better understand impact of the hip in LBP.

Purpose: To describe hip physical examination findings in adolescent and young adults seeking treatment for LBP to understand prevalence and differentiating factors between patients with and without accompanying hip findings. Hypotheses1: positive hip examination test(s) will be found in 20% of consecutive adolescent and young adult patients presenting with LBP. Hypotheses 2: Validated outcome tools that measure pain and function will be unique in a cohort of consecutive patients with LBP with positive hip examination tests when compared to patients without this finding. Hypothesis 3: Physical examination tests can identify patients with potential hip disorders when presenting symptoms include LBP and posterior pelvic pain associated with lateral thigh, groin, or lower extremity pain. Literature-based rationale: Hip and spine disorders are causes of impairment and disability. Overlapping symptoms can make them difficult to distinguish. There is currently no prospective data on hip physical findings in adolescents and young adults presenting with LBP. Understanding this relationship will drive treatment options and recommendations.

Design: Description: Prospective observational cohort study completed in a tertiary university setting. Subjects: Consecutive patients ages 10 to 23 presenting for evaluation of LBP. Methods: 24 adolescents and young adults completed validated pain and function questionnaires including: pain diagram, numeric pain rating (NPR), modified Oswestry Index (mODI), Rolland-Morris (RMQ), UCLA activity score, modified Harris Hip Score (mHHS), StarT Back Screening Tool, and HOOS Hip Survey. Hip and spine physical examination findings were recorded and described. Comparisons were made in pain and function in people with hip internal rotation < 20° to those with >20° of motion. Pain and function in people with and without a positive provocative hip test were compared. Ethics: Institutional Review Board approval was obtained for all participating institutions. Interventions: None. Measures: NPR, mODI, RMQ, UCLA activity score, mHHS, The Keele StarT Back Screening Tool, and HOOS Hip Survey. Analysis: For normally distributed continuous data, summary statistics are mean ± standard deviation. Ordinal scaled or non-normally distributed continuous variables are reported as median with interquartile range defined as [25th percentile, 75th percentile]. Categorical variables are reported as number of patients. An alpha level of < 0.05 was used to determine statistical significance. All analyses were conducted using SAS. Results: Data Presentation/Statistical Analysis/Significance: 24 consecutive patients (18 women, 6 men) with a mean age of 18.9 years (SD±3 years) and mean BMI of 23.7 kg/m2 (SD±5 kg/m2) were enrolled. On physical examination 1) 3 (12.5%) displayed an antalgic gait, 2) 13 (54%) had hip internal rotation < 20°, 3) 5 (20%) had 1, 6 (24%) had 2 and 10 (40%) had 3 positive provocative hip tests. As compared to patients with normal range of motion, patients with reduced
Determining recruitment patterns of continence and micturition reflexes in response to multichannel microstimulation of the sacral dorsal root ganglia

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Objectives
The primary objective of this work was to identify patterns of lower urinary tract (LUT) afferent recruitment resulting from microstimulation of the sacral dorsal root ganglia (DRG). A secondary objective was to measure functional storage and voiding behavior resulting from coordinated multichannel microstimulation of sacral DRG.

Design
In two cats, nerve cuffs were placed on the pudendal nerve and its branches (rectal perineal, caudal rectal, and sensory nerves) as well as the pelvic nerve. Bladder, urethral and rectal pressure transducers were used to monitor physiological responses to electrical stimulation. Isoflurane anesthesia was used during surgical implantation and electroneurogram (ENG) recording, while alpha-chloralose anesthesia was used during functional testing to prevent inhibition of continence and micturition reflexes. Following a laminectomy, 32-channel Utah microelectrode arrays were implanted in the S1 and S2 DRG. Antidromic action potentials were recorded from implanted nerve cuffs in response to single channel stimulation of DRG electrodes. Functional testing was performed at parameters ranging from 2-30Hz and 3-50 μA to quantify bladder or external urethral sphincter contractions in response to stimulation.
**Results**

DRG microstimulation generated selective activation of the pelvic nerve with 8 electrodes (9.6μA +/- 3.0μA average threshold), the pudendal nerve with 5 electrodes (18.7μA +/- 10.0μA average threshold), the sensory nerve with 12 electrodes (17.1μA +/- 8.5μA average threshold) and the deep perineal nerve with 1 electrode (threshold of 15.3 μA). No selective responses were seen on the caudal rectal and rectal perineal nerves. Functional testing evoked selective bladder contractions on 45/128 electrodes between both S1 and S2 DRG. The mean bladder contraction magnitude was 6.3 mmHg +/- 2.4mm Hg with the largest contraction being 14 mmHg. Single channel stimulation did not elicit significant EUS contractions. Sustained bladder contractions of 8mm Hg were recorded when multiple selective channels were stimulated for 30 seconds.

**Conclusions**

Microstimulation of the DRG can elicit micturition reflexes to cause voiding. Sustained contractions show promise that physiological functions can be achieved through DRG microstimulation of the micturition reflex.

**Research Study with Best Paper Award Abstract**

People with spinal cord injury (SCI) face significant challenges with urinary tract function resulting from the loss of supraspinal control. These complications have led to the development of several clinical devices focused on improving bladder management, with the goals of decreasing urinary tract infections and healthcare costs and improving the quality of life for people with SCI. However, many of the clinical methods and devices to control and manage bladder function are imperfect. Electrical microstimulation could be an effective method to address these issues, but no devices are currently available. One potential location for microstimulation of afferent fibers involved in the lower urinary tract (LUT) are the dorsal root ganglia (DRG). Feline LUT reflex pathways primarily travel through the S1-S3 DRG. Previous research has shown that electrical stimulation of pudendal nerve afferents can elicit continence reflexes through activation of the dorsal nerve of the penis (branch of pudendal nerve). Sensory input from the pelvic nerve is important to fully void the bladder through LUT reflexes. The primary aim of these experiments was to identify recruitment patterns of LUT afferents in response to DRG microstimulation. A second aim of these experiments was to combine single channels with the same physiological function and stimulate them to attempt to elicit greater physiological responses (both micturition and continence).

All experimental protocols were approved by the University of Pittsburgh’s Institutional Animal Care and Use Committee. Detailed surgical procedures and experimental methods common to the aims have been described previously (Bruns et al. 2015) and are summarized briefly here. Surgical procedures were performed under isoflurane anesthesia and the animals were mechanically ventilated. The abdomen was opened and a dual-lumen catheter was placed in the bladder to monitor bladder pressure and to control bladder volume. While the abdomen was open, a custom nerve cuff electrode was placed on the pelvic nerve. The abdomen was closed in layers, the animal was placed in a prone position, and the pudendal nerve and its branches were dissected free. Custom nerve cuff electrodes were placed on the pudendal, rectal perineal, sensory, caudal rectal and deep perineal nerves. After a sacral laminectomy, microelectrode arrays (Utah arrays, 32 channels per device, 400 μm interelectrode spacing) were implanted into the S1 and S2 DRG unilaterally. Microstimulation was delivered through individual DRG electrodes with stimulus amplitudes ranging from 3 to 50 μA. Electroneurogram (ENG) signals were recorded from the nerve cuffs and stimulus-triggered averaging was used to examine peripheral nerve activity for the presence of compound action potentials. Functional testing to determine bladder and EUS responses were conducted under alpha-chloralose anesthesia to avoid suppression of spinal reflexes. Functional testing involved single channel stimulation of each of the electrodes on the arrays in both S1 and S2 at different stimulus parameters from 2 – 50 Hz and 3 - 50 μA. Additionally, combinations of channels that elicited similar physiological responses were tested to note changes in the physiological response.
ENG data showed selective recruitment of the pelvic nerve by 8 electrodes at an average threshold of 9.6 μA +/- 3.0 μA. The pudendal nerve was selectively stimulated by 5 electrodes at an average threshold of 18.7 μA +/- 10.0 μA. The branches of the pudendal that were selectively stimulated include the sensory nerve, with 12 selective electrodes at an average threshold of 17.1 μA +/- 8.5μA, and the deep perineal branch, with one selective electrode at a threshold of 15.6 μA. No selective responses were seen on the caudal rectal and rectal perineal nerves.

Results from the functional testing of the two animals showed that single channel stimulation evoked contractions of the bladder without simultaneous EUS contraction on 45/128 electrodes from S1 and S2 of both animals. Amplitudes of at least 20 μA were needed for 97% of the bladder contractions to occur. The average magnitude of bladder contraction was 6.3 mmHg +/- 2.4 mm Hg. The largest magnitude bladder contraction observed was 14 mm Hg. Combining two channels that individually showed large bladder contractions at 10 μA and 30 Hz for a duration 30 seconds showed a sustained 8 mmHg bladder contraction. These results demonstrate that micturition reflexes can be evoked through microstimulation of sensory neurons in the sacral DRG. Single channel microstimulation did not elicit selective EUS contractions on any electrode. We also found that in some cases, simultaneous stimulation on multiple channels at subthreshold currents could elicit a physiological response similar to stimulation at suprathreshold currents on individual channels.

Several limitations occurred in this study. In the second experiment it was challenging to record reliable intraurethral pressures due to challenges in placing the transducer. Instrumentation of the various nerve branches was also difficult and led to poor recording performance in several cases. It is also possible that difficulties in eliciting large functional responses could have been due to compression of the nerves from the nerve cuffs themselves. A possible way to improve on this research in the future would be to include the L7 DRG in the study as we found some evidence in our study that stimulation of L7 could elicit EUS contractions.

Presence of Overflow Movements in Children with Traumatic Brain Injury Correlates with Corpus Callosum Segment Size

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Objectives
Children with traumatic brain injury (TBI) often have grossly normal physical exams despite persistence of cognitive and behavioral concerns. The primary objectives of this study were to characterize subtle motor movements in children TBI and to evaluate the relationship between overflow movements and corpus callosum (CC) morphology.

Design
Data were collected from 24 children at least one year after mild-complicated to severe TBI and 19 age and sex-matched controls (ages 9.93-18.65 years). Overflow movements were assessed using the Physical and Neurological Examination for Subtle Signs (PANESS). Using MPRAGE images, the CC was divided into five segments using an automated algorithm, and segment areas were computed. Independent t-tests evaluated between-group differences for PANESS scores and CC areas. Partial correlations controlling for age evaluated the relationships between PANESS scores and a) CC segment areas and, b) secondarily, performance on speeded cognitive tasks.

Results
Children with TBI had more proximal overflow movements than controls (p= 0.011). Children with TBI had smaller areas for four of five CC segments (rostral body p= 0.018, midbody p= 0.009, isthmus p= 0.043, splenium p= 0.044). In children with TBI, there was a negative correlation between proximal overflow and area of three CC segments
(midbody r = -0.535, p = 0.022; isthmus r = -0.548, p = 0.018; splenium r = -0.482, p = 0.043). In children with TBI, there was also significant correlation between proximal overflow and speeded cognitive tasks (r = -0.481 to -0.663, p = 0.001-0.027).

Conclusions
Children with TBI show subtle motor exam findings in the chronic phase of recovery which are associated with CC size in regions that project to premotor and primary sensorimotor cortices and also correlate with cognitive performance. This provides an opportunity to increase sensitivity of physical examination both for milder motor effects of TBI and as a screening to determine which children may benefit from more extensive cognitive/behavioral evaluations.

Research Study with Best Paper Award Abstract
Background: Traumatic brain injury (TBI) is a leading cause of disability in children with resulting deficits in motor functioning, cognition, academic performance, and participation in daily activities. Severity of these deficits varies amongst affected children, and often the physical exam can be grossly normal despite the presence of significant cognitive and behavioral concerns. Subtle motor exam findings have been described in other childhood brain disorders associated with cognitive/behavioral dysfunction, such as ADHD and Autism. One type of subtle finding, overflow movements, is thought to be linked to corpus callosum (CC) function. Overflow movements have not been examined in children with TBI; however, given the high rate of CC injury in pediatric TBI, overflow movements may represent a subtle physical examination finding in children with TBI with relevance for broader sequelae of injury.

Purpose: The primary objectives of this study were to characterize subtle motor movements in children with TBI and to evaluate the relationship between overflow movements and CC morphology. A secondary objective was to evaluate the relationship between overflow movements and cognitive performance.

Hypotheses: 1. Children with TBI will demonstrate more overflow movements compared to typically developing controls. 2. CC segment area will be smaller in children with TBI compared to controls. 3. In children with TBI, CC segment area will inversely correlate with the number of observed overflow movements. 4. In children with TBI, overflow movements will correlate with cognitive performance.

Design: This is a cross-sectional observational study. Data were collected from children with a history of mild-complicated to severe TBI occurring at least one year prior and age and sex-matched typically developing controls. Institutional Review Board approval was obtained.

Participants: 24 children with TBI (Ages 9.93-18.65 years, mean=15.07 years, 17 males) and 19 controls (Ages 11.92-16.82 years, mean age=15.32 years, 15 males) were included. All participants with TBI had a history of loss of consciousness (lasting from seconds to >24 hours) and post-traumatic amnesia.

Measures:
Motor Evaluation
The Physical and Neurological Examination for Subtle Signs (PANESS) was designed for use in neurodevelopmental pediatric populations as a measure of balance, speed and rhythmicity of repetitive movements, and presence of overflow movements. Of primary interest for this study was the number of overflow movements (proximal, mirror, and oro-facial) during timed motor tasks (foot tap, foot heel-toe tap, hand pat, hand pronate/supinate, finger tap, and finger sequencing). Each type of overflow movement was noted as present or absent for each task.

CC imaging data
Imaging analyses was completed on high-resolution magnetization prepared rapid gradient recalled echo images (MP-RAGE) which were obtained on a 3 T Philips Gyroscan NT for 19 of the participants with TBI and 11 of the controls. The CC was manually delineated in the midsagittal plane and then divided into five segments (genu, rostral body, midbody, isthmus, and splenium) using an automated algorithm. Segment area was computed for each of the five segments and for the entire CC. A modified algorithm was developed for scans with CC lesions (n=5) which allowed accurate calculation of segment areas despite atypical morphology.
Cognitive Performance
Speeded cognitive function was assessed with verbal fluency and coding tasks.
Analysis: Analyses were completed using SPSS. Independent t-tests were performed to evaluate between-group differences for PANESS scores and CC areas. Given the range of ages included, a bivariate correlation was completed and showed a relationship between age and both PANESS scores and CC areas within the TBI group. Thus, partial correlations controlling for age were used to evaluate for relationships between PANESS scores and CC areas. As a secondary analysis, partial correlations between proximal overflow and cognitive tasks were evaluated.

Findings: Children with TBI had more proximal overflow movements than did controls (p = 0.011). There was no between-group difference in mirror (p=0.137) or oro-facial overflow (p = 0.954). Children with TBI had smaller areas for four of five CC segments (rostral body p = 0.018, midbody p = 0.009, isthmus p = 0.043, splenium p = 0.044) and total CC total area (p= 0.020). In children with TBI, after controlling for age, there was a negative correlation between proximal overflow and three CC segment areas as well as CC total area (midbody r = -0.535, p = 0.022; isthmus r = -0.548, p = 0.018; splenium r = -0.482, p = 0.043; total area r = -0.541, p = 0.020). In children with TBI, there was also a significant correlation between proximal overflow and speeded cognitive tasks (r=-0.481 to -0.663, p = 0.001 to 0.027).

Limitations: Imaging was not available for 5 TBI and 8 control participants. Among the groups with imaging data, the groups were no longer matched which could contribute to the group differences in CC areas but does not affect other findings. PANESS was administered over time by multiple different examiners; however, all examiners were trained in the same fashion and evaluated for consistency and reliability in ratings prior to administering the PANESS for research purposes.

Importance: These data demonstrate that children with TBI show subtle motor exam findings in the chronic phase of recovery. This may provide an opportunity for clinicians to increase the sensitivity of the physical examination for late effects of TBI. Furthermore, we identified that the presence of proximal overflow movements is associated with smaller CC areas in regions that are known to project to premotor and primary sensorimotor cortices. Thus, injury to the CC, whether primary from TBI or secondary due to Wallerian degeneration, likely is related to the presence of these subtle motor signs. Consistent with prior reports of an association between CC injury in pediatric TBI and cognitive dysfunction, these abnormal overflow movements were also associated with slower cognitive speed. Therefore, clinicians may be able to use simple physical examination maneuvers as part of a screening to identify which children are likely to benefit from more extensive cognitive/behavioral evaluations.

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USE OF AN ARTIFICIAL SPINAL CORD IN THE TREATMENT OF SPINAL CORD INJURY

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Objectives
The goal of this study is to combine a number of strategies for spinal cord repair and arrange them to mimic the normal organization of the spinal cord to create an ‘artificial spinal cord’. We have attempted to replace damaged elements (neurons, support cells) and encourage the growth of ascending and descending axons while also
addressing injury-induced changes. We hypothesize that the artificial spinal cord will cause functional improvement and morphological changes in the spinal cord after producing a spinal cord injury through spinal cord segment removal.

**Design**
Twelve male Lewis rats were used in this study and were randomly assigned to one of three groups. The first group acted as controls and underwent a sham surgery consisting of a laminectomy from T9-T11. The second group underwent a spinal cord segment removal and a blank hydrogel was implanted. The third group underwent a spinal cord segment removal and the hydrogel implanted contained stem cells, neurotrophic growth factors, an enzyme to prevent scar formation around the injury site, and a scaffold base of aligned electrospun fibers. Outcome measures are being assessed by BBB score, beam test, Hargraves test, and the inclined plane test. Data will be analyzed via a two-way ANVOA with a Scheffe post hoc comparison. Statistical significance is considered to be present at $P < 0.05$.

**Results**
The spinal cord injured rats have undergone environmental enrichment, exercise, and behavioral testing in the weeks since their injury. Performance in Group 3 (artificial spinal cord) has improved and is better than Group 2 (blank hydrogel) but significance has not yet been reached. Testing is continuing in these rats.

**Conclusions**
This study is still in progress. The combination of several treatment approaches, that have each previously demonstrated functional improvement, could lead to results which would greatly benefit the development of effective treatment for individuals with spinal cord injuries.

**Research Study with Best Paper Award Abstract**

**Objectives**
Spinal cord injury (SCI) has devastating consequences in terms of physical disabilities, and enormous emotional, personal, and fiscal tolls for both patients and their loved ones. Damage to the spinal cord includes the destruction of neurons and support cells and damage to ascending and descending axons that prevents signal transmission. Barriers to repair the injury include scar formation and the lack of a permissive substrate from axonal growth for the axons that remain near the injury site. Experimental animal studies of spinal cord injury to replace one or more of these components often results in some functional improvement. However, no one has attempted to replace all of these elements and create an artificial spinal cord that replicates the organizational structure of the spinal cord, with neuron cell bodies surrounded by ascending and descending pathways, while also addressing injury-induced changes. In order to develop an effective treatment for people with spinal cord injury, the goal of this project is to evaluate an artificial spinal cord to repair spinal cord injury in rats.

**Specific Aims and Hypotheses:**
Our hypothesis is that the artificial spinal cord will cause functional improvement and morphological changes in the spinal cord after inducing a SCI through spinal cord segment removal.

**Aim 1.** To compare the function of the rats after spinal cord segment removal in 3 groups (4 rats/group) that received: 1) artificial spinal cord transplant; 2) sham surgery consisting of a laminectomy only; 3) hydrogel transplant without any cells or factors. The artificial spinal cord or hydrogel was grafted immediately after spinal cord segment removal. All rats were behaviorally tested and exposed weekly to an enriched environment.

**Aim 2:** To evaluate the morphological changes in the spinal cord after sham surgery or spinal cord segment removal with grafting of an artificial spinal cord or hydrogel. The artificial spinal cord will be examined for the survival of cells, ingrowth of axons and myelination of axons. The injury site in the rats that received the hydrogel will be similarly examined. The cell types present at the injury site will be characterized.
**Design**

Twelve adult Lewis inbred rats were randomly assigned to one of three groups:

1. Laminectomy only (Sham surgery).

2. Segment removal and implantation of a hyaluronic acid hydrogel (without cells or neurotropic factors)

3. Segment removal and implantation of the artificial spinal cord.

All rats were anesthetized to a surgical plane with isoflurane and a laminectomy was performed at T9-11.

The artificial spinal cord contained the following components:

1. Electrospun hyaluronic acid (HA) scaffolds: Electrospun material provides channels that direct axons and processes of stem cells to grow in a straight line. Axons need a substrate for growth and cannot grow through the fluid-filled cavity that forms after spinal cord injury.

2. Olfactory Mucosal Stem Cells: Human olfactory stem cells form synaptic connections with endogenous cells in spinal cord injured rats. Olfactory mucosal stem cells increase function after spinal cord injury or head injury. Olfactory mucosal autografts containing stem cells produces functional improvement in people with chronic spinal cord injury when given appropriate rehabilitation. These cells were placed on the center scaffolding to direct the outgrowth of processes.

3. Gradients of neurotrophic factor-containing microspheres: To encourage the growth of sensory axons, one of the layers of electrospun scaffolding contained gradients of brain derived neurotrophic factor (BDNF). Gradients of glia cell line derived neurotrophic factor (GDNF) were used to encourage the growth of motor axons. The neurotrophic factor microspheres within the two separate electrospun HA scaffolds provided guidance for ascending and descending endogenous axons.

4. Olfactory Ensheathing Cells (OEC): OECs improve function in spinal cord injured rats by myelinating axons for improved signal conduction and propagation. This allows the embedded OECs to migrate into the adjacent layers that contain axons that grow into the artificial spinal cord.

5. Chondroitinase ABC: A chemical (chondroitinase ABC) was used to prevent scar formation in the artificial spinal cord. Chondroitinase is known to disrupt the scar and prevent its formation.

The above-mentioned components were surrounded by a biocompatible customized hyaluronic acid hydrogel.

Rats were checked twice daily and bladders expressed as needed. Supplemental food (kale, corn, cereal, soft chow, Ensure) was given to help maintain weight. Cages were placed partially on a heating pad to help the rats maintain adequate body temperature. Rats were exposed to an enriched environment for 4 hours/week. Functional testing includes the beam test (successively narrower beams are used until the rat can no longer maintain balance), the Hargreaves thermal sensitivity test (measures how long the rat takes to move its hindpaw after heat is applied, to footpad and has automatic cut-off so there is no skin damage), the BBB locomotor test and subscore, and the inclined plane (highest angle in which the rat can maintain balance). The neurological testing is currently ongoing. At the conclusion of the study, the rat will be perfused with saline then 4% paraformaldehyde and the artificial spinal cord will be analyzed histologically for the presence of host axons and axonal myelination, and cell survival.

**Results**

We have preliminary results for the first 5 weeks following the surgeries. The rats receiving the artificial spinal cord
are performing better in all tests but significance has not yet been reached. Sham surgeries in which the spinal cord was not injured revealed normal function by 2 weeks after surgery. Testing is currently ongoing.

**Conclusions**
This study is still in progress. The combination of several treatment approaches, that have each previously demonstrated functional improvement, could lead to results which would greatly benefit the development of effective treatment for individuals with spinal cord injuries.

**Ultrasound Determined Knee and Hip Muscle Parameters Predict Formalized Strength Measurements in Adults with Knee Osteoarthritis**

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**Objectives**
Knee osteoarthritis (OA) is a highly prevalent and disabling disease, and interventions aimed at slowing its progression are urgently needed. Research has shown lower quadriceps strength in knee OA patients than matched controls and that higher knee extensor strength predicts lower pain and better physical function. Less is known regarding the role of hip muscle strength in symptomatic knee OA. However, there is a strong theoretical basis for its importance since hip musculature determines knee joint position.

We hypothesize that measuring muscle size and fat infiltration of hip abductors, hip adductors, and knee extensors with ultrasound on adults with knee OA will be feasible and correlate with formal strength measurements.

**Design**
We enrolled nine subjects (18 knees) with unilateral knee OA in this cross-sectional study. Muscle thickness and echo intensity of the quadriceps, hip abductors, and hip adductors were measured with ultrasound. Strength measurements were obtained with a handheld dynamometer. Pearson correlation coefficients were determined relating muscle thickness and echogenicity to strength. Parameters for the symptomatic and asymptomatic sides were compared.

**Results**
Ultrasound-measured quadriceps muscle thickness correlates with knee extension torque \( r=.70, p=.001 \). Hip abductor muscle thickness correlates with hip abduction torque \( r=.70, p=.001 \). Hip adductor muscle thickness correlates with hip adductor torque \( r=.43, p=.07 \). Ultrasound-measured echogenicity negatively correlated with torque for hip adductors \( r=-.62, p=.006 \) but was not significant for other muscle groups. No significant difference in muscle thickness or force was found between symptomatic and asymptomatic sides.

**Conclusions**
This is the first report of the correlation between ultrasound muscle measures and strength in adults with knee OA. Ultrasound-measured muscle thickness strongly correlated to formalized torque measurements of knee extensors, hip abductors, and hip adductors. Obtaining these measures in a clinical setting is feasible and may help guide exercise therapy prescription, as well as provide a longitudinal biomarker.

**Research Study with Best Paper Award Abstract**

**Objectives**
Knee osteoarthritis (OA) is a highly prevalent and disabling disease. Millions of people around the world suffer from pain associated with knee OA and are often inhibited from completing simple activities of daily living because of it. Clearly, interventions aimed at slowing or stopping OA progression are urgently needed. In this regard,
quadriceps muscle strengthening has received a fair amount of critical study over the past decade. Previous studies have concluded that patients with knee OA have lower quadriceps strength than matched controls, and that higher grades of knee extensor strength predict lower pain and better physical function. Thus, strengthening of the quadriceps has become a mainstay of physical therapy prescriptions for knee OA patients. Much less is known about the role of hip muscle strength in symptomatic knee OA, but there is a strong theoretical basis for its importance. While knee extensor strength can modify the absolute forces and the rate of force development across the knee joint during gait, the hip musculature is more important in determining knee joint position by controlling the proximal femur at the level of the pelvis. Weakness or poor neuromuscular control of the proximal femur will lead to inaccurate positioning of the distal end of the femur at its articulation with the tibia.

The objective of this study was to determine if there is a relationship between strength, as measured by handheld dynamometry, and muscle thickness and fat infiltration, as determined by ultrasound. We also attempted to determine if these measurements differed between the symptomatic and asymptomatic legs in these unilateral knee OA subjects.

The central hypothesis is that using ultrasound to measure muscle size and fat infiltration of hip abductors, hip adductors, and knee extensors in adults with knee OA will be feasible and correlate with formal strength measurements performed with handheld dynamometry. The secondary hypothesis in this study is that ultrasound-measured muscle size and fat infiltration will differ between the symptomatic and asymptomatic legs.

**Design**

This project is a cross-sectional analysis of adults with symptomatic unilateral knee OA. We compared muscle strength to ultrasound-measured muscle thickness and fat infiltration in the knee extensors, hip abductors, and hip adductors.

We enrolled nine subjects (18 knees) with unilateral knee OA. All subjects were above 50 years of age and had radiographic and symptomatic evidence of knee OA. There were four female and five male subjects. Four subjects reported left-sided symptomatic knee OA while five reported right-sided symptomatic OA. Demographic and baseline information including age, gender, height, weight, knee pain as measured with the numeric rating scale (NRS), WOMAC Osteoarthritis index, Lower Extremity Activity Scale (LEAS), and duration of symptoms was documented before beginning the protocol.

For each subject, muscle thickness and echo intensity of the quadriceps, hip abductors, and hip adductors were measured with ultrasound. Placement of the probe at the three locations on each leg was done systematically as to obtain consistent intra- and inter-subject measurements. Three images were taken at each location and the thickness and echogenicity results were averaged for each muscle group. Strength measurements (peak force and torque) were obtained with a handheld dynamometer for these same muscle groups. Optimal placement of the dynamometer and positioning of the subject were determined by literature review of similar strength testing. Each muscle group was tested three times, and those results were subsequently averaged.

Baseline characteristics were described using simple descriptive statistics. Pearson correlation coefficients were determined for muscle thickness and echogenicity as they relate to strength. We considered a Pearson’s correlation between .40 and .69 as a strong relationship and correlation >0.70 as a very strong relationship. The muscle parameters for the symptomatic and asymptomatic side were also compared using two sample T-tests.

**Results**

Mean subject age was 64 (SD = 7.1), with mean BMI 25.9 (SD = 3.8), and mean baseline pain 4.0 (SD = 1.9). WOMAC was widely variable, with mean 22.9 (SD = 15.9). Ultrasound-measured quadriceps muscle thickness had a very strong relationship with knee extension force (r=.79, p < .001) and torque (r=.70, p=.001). Similarly, ultrasound-measured hip abductor muscle thickness had a very strong relationship with hip abduction force (r=.71, p=.001) and torque (r=.70, p=.001). Ultrasound-measured hip adductor muscle thickness had a strong relationship with hip adductor strength (r=.45, p=.06) and torque (r=.43, p=.07). Ultrasound-measured echogenicity had a
strong negative relationship with force and torque for hip adductors ($r=-.62$, $p=.006$) but did not reach significance for other muscle groups. There was no significant difference in muscle thickness or force between symptomatic and asymptomatic sides for any muscle group.

The main limitation of this study was the low number of study participants. It is possible that more subjects would have allowed us to detect differences in strength and ultrasound parameters between the symptomatic and asymptomatic sides.

**Conclusions**

This is the first report of the correlation between ultrasound muscle measures and strength in adults with knee OA. In this population, muscle thickness as measured by ultrasound is strongly correlated to formalized force and torque measurements in the knee extensors, hip abductors, and hip adductors. Obtaining these measures in a clinical setting is feasible and may help guide exercise therapy prescription. In the future, a clinician could use these measures to quickly identify changes in muscle thickness and echogenicity and relate them to changes in the pain and function of knee OA patients from visit to visit. Thus, it is possible that one day these measures could effectively and reliably be used as biomarkers capable of being followed longitudinally.