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COMPLETE ABSTRACTS

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Poster #	Title	Presenting Author
1	A pilot RCT to test the effect of Lokomat-applied force fields on functional walking skills in people with motor-incomplete spinal cord injury.	Tania Lam, PhD, BScPT
2	Daylong movement monitoring to differentiate healthy from impaired infant development.	Beth Smith, PT, DPT, PhD
3	Quantifying the feasibility of pairing tDCS with standard physical therapy following neurological insult using clinical and robotic assessment tools	Addie Middleton, DPT
4	Activity-dependent mechanisms of neural circuit plasticity during limb-overuse following ischemic stroke	Esther Nie
5	Frontal-Subcortical Function and Use of Assistive Speech Devices for Aphasia	Amit Chaudhari, BA
6	Potential therapeutic effects of sensory tongue stimulation combined with task-specific therapy in people with spinal cord injury	Raza Malik, BKIN / MSc Student
7	Does paired stimulation of cutaneous and proprioceptive receptors enhance motor performance of a skilled walking task?	Amanda Chisholm, PhD
8	A novel approach to quantifying changes in locomotor EMG patterns in incomplete spinal cord injury	Brad Farrell, PhD
9	Measurement of volitional muscle activity initiation and cessation after spinal cord injury	Barry McKay, BS
10	Acute and post-acute assessment of postural control and cognitive efficiency following concussion.	Laurie King, PhD, PT
11	A quantitative method for measuring bilateral arm activity via accelerometry	Ryan Bailey, MSOT
12	Spatial cognitive function of the right insula: A study with stroke survivors	Peii Chen, PhD
13	AMES + brain stimulation for treatment of hand plegia: A proof-of-concept study	Paul Cordo, PhD
14	Reorganization of the locomotor network in Parkinson patients with freezing of gait	Fay Horak, PT, PhD
15	Targeted exercises to increase cortical influence over spinal reflexes	Noam Harel, MD, PhD
16	Damage and recovery following white matter stroke: a key role for age	Shira Rosenzweig, PhD
17	Feasibility of Bilateral Arm Training in the Subacute Setting	Sandy McCombe Waller, PhD, PT
18	Bilateral reach training following a unilateral ischemic injury to the caudal forelimb area (CFA) of motor cortex in rats	Anthony Dutcher, B.A. Psychology
19	Impact of motor cortical stimulation timing during planar robotic training on neuroplasticity in older adults.	Crystal Massie, PhD, OTR
20	Transcallosal effects of chronic below-elbow arm amputation: a pilot study	Erika Y. Breceda
21	Graph Theoretical Analysis of Resting State EEG in Post-acute Stroke Recovery	Ron Goodman, PhD

22	Reliability of Negative Bold in the Primary Motor Cortex	Keith McGregor, PhD
23	Mechanisms of rhythm and pattern generation of the human lumbar spinal cord tested by epidural stimulation	Karen Minassian, PhD
24	Alternating reflex modulations by spinal neural circuits ‘outside' the human lumbar locomotor pattern generator	Ursula Hofstoetter, PhD
25	Educate, Train, Treat, Track: Bringing state of the art care to our Military with TBI	Stephanie Maxfield-Panker
26	Premotor cortical stimulation in stroke rehabilitation: neural mechanisms of recovery	Nicole Varnerin, BSE
27	Diffusion Tensor Imaging exhibits more proximate and reliable Transcranial Magnetic Stimulation measures compared to fMRI in stroke	David Cunningham, MS
28	Individually-Targeted Transcranial Direct Current Stimulation Enhances Fluency in Patients with Chronic Non-Fluent Aphasia	Catherine Norise, BA
29	Activation changes induced by mnemonic strategy training during memory encoding and retrieval in patients with mild cognitive impairment	Benjamin Hampstead, PhD
30	Neurochemical predictors of motor recovery in stroke	Carmen Mihaela Cirstea, MD, PhD
31	Effects of feedback to enhance self-efficacy on paretic hand use in chronic stroke.	Yi-An Chen, MS, OT
32	Home-based robot-assisted ankle rehabilitation for chronic stroke survivors	James Lynskey, PT, PhD
33	Central plasticity of segmental cutaneous nociceptive primary afferents is associated with evoked nociceptive hypereflexia after hemisection spinal cord injury in rats	Keith Tansey, MD, PhD
34	Central plasticity of segmental cutaneous nociceptive primary afferents is associated with evoked dysautonomia after cervical spinal cord injury in rats	Keith Tansey, MD, PhD
35	Motor control changes in incomplete SCI generated by adding tonic transcutaneous spinal cord stimulation to robotic locomotor training: a test of concept study	Keith Tansey, MD, PhD
36	Real-time optimization of sensory stimulation to improve walking metrics after spinal cord injury	Keith Tansey, MD, PhD
37	Study Protocol: Rationale and methods for a pilot study of brain imaging to predict response to robotic rehabilitation during inpatient rehabilitation	Michael Dimyan, MD
38	Improved motor performance in chronic spinal cord injury following upper-limb robotic training	Mar Cortes, MD
39	Initiating Word-Finding Trials with Left-Hand Movement during Anomia Treatment Remaps Frontal Language and Executive Mechanisms	Bruce Crosson, PhD
40	Facilitating neuronal recovery after pediatric traumatic brain injury using optogenetics	David Glover, BS
41	Implementation of a multi-center, international, randomized clinical trial in sub-acute stroke patients using wireless health technology	Andrew Dorsch

42	Development of Virtual Games with Functional Electrical Stimulation for Post-Stroke Hemiplegia	Michael Fu, PhD
43	Influence of elbow angular spasticity zones on one-trial motor learning in chronic stroke	Mindy F. Levin, PT, PhD
44	Altered obstacle avoidance behaviour in individuals with good arm recovery after stroke	Mindy F. Levin, PT, PhD
45	Does accelerometer-based feedback increase walking activity during in-patient rehabilitation post-stroke? Preliminary results from a randomized controlled trial.	Avril Mansfield, PhD
46	Intensity-dependent effects of tDCS on corticospinal excitability in chronic SCI	Mar Cortes, MD
47	Neurophysiological signatures of proximal and distal recovery after stroke	Heidi Schambra, MD
48	Instrumented Gait Analysis to Differentiate Patients with Mild Cognitive Impairment	Marcia Thompson, PT, DPT, DSc
49	Turning Stability in people with Parkinson's disease	Sabato Mellone, PhD
50	Alterations in upper limb muscle synergies with level of motor impairment in chronic stroke survivors	Jinsook Roh, PhD
51	Feasibility of relating continuous monitoring of turning mobility to fall risk and cognitive function	Martina Mancini, PhD
52	Learning strategies of young preterm and term infants	Barbara Sargent, PhD, PT, PCS
53	Measuring Cortical Physiology in Stroke Patients with Severe Arm Impairment	Michelle Harris-Love, PT, PhD
54	Time Course and Magnitude of Motor Learning during Gait Rehabilitation - a Preliminary Study	Trisha Kesar, PT, PhD
55	From BCI to AAC and back: towards practical augmentative and alternative communication systems using brain-computer interfaces	Daniel Bacher, MS
56	How does the brain support the recovery of hand function for grasping following surgical hand replantation or transplantation?	Kenneth Valyear, PhD
57	Wearable audio-biofeedback system for gait rehabilitation of subjects with Parkinson's disease	Lorenzo Chiari, PhD
58	Correlation Between Gait Parameters and Balance in Very Young Children. Correlation Between Gait Parameters and Balance inVery Young Children.	Paola Pergami, MD, PhD
59	Changes in resting-state functional connectivity following BCI-EEG based intervention in sub-acute and chronic stroke patients	Vivek Prabhakaran, MD, PhD
60	Peripheral nerve injury induces long-term synaptic depression in rat somatosensory cortex	Galit Pelled, PhD

Poster #1

A pilot RCT to test the effect of Lokomat-applied force fields on functional walking skills in people with motor-incomplete spinal cord injury.

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Background: People with motor-incomplete spinal cord injury (m-iSCI) can recover basic walking function, but still have difficulty performing the skilled walking required for everyday environments. We hypothesize that a robotics-based gait rehabilitation strategy founded on principles of motor learning will be effective for improving skilled walking in people with m-iSCI. *Objectives:* To evaluate the feasibility and effect of body-weight supported treadmill training (BWSTT) combined with Lokomat-resistance in people with m-iSCI. *Methods:* 15 individuals with chronic (>1 year) m-iSCI were randomly allocated to BWSTT with Lokomat-resistance (Loko-R) or conventional Lokomat-assisted BWSTT (Control). Training sessions were 45 minutes, 3 times/week for 3 months. We compared skilled walking capacity (Spinal Cord Injury-Functional Ambulation Profile, SCI-FAP), as well as 10-meter walk speed, and 6-minute walking distance between groups at baseline, post-training, and 1- and 6-months follow-up. *Results:* Training was well tolerated by both groups although participants in Loko-R tended to report higher levels of perceived exertion during training. At baseline, there were no significant between-group differences. Participants in the Loko-R group performed significantly better in the SCI-FAP compared to Control at post-training and in follow-up assessments. Both groups showed improvements in walking speed and distance with training, but there were no between-group differences. *Conclusions:* Performance in over ground skilled walking improved even though those tasks were not specifically trained, suggesting task- and context-related generalization of locomotor training effects. This study provides evidence for the potential effectiveness of gait training approaches, such as BWSTT with Lokomat-resistance, that are based on principles of motor learning.

Poster #2

Daylong movement monitoring to differentiate healthy from impaired infant development.

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Introduction: Very early identification of impaired infant neuromotor control is needed in order to initiate and target intervention. Our goal is to use full-day movement monitoring with small inertial sensors on infants' legs to differentiate healthy and impaired neuromotor control.

Methods: We collected a full day (8-13 hours) of leg movement activity from 12 typically-developing infants, ages 1 to 12 months. Infants were measured 3 times each, 2 months apart. Tri-axial accelerometer and gyroscope data were collected at 20 Hz from sensors at the ankles. Although movement detection based on acceleration was sensitive to leg movement, some false positives were detected due to linear acceleration from extraneous background movement. Gyroscope data appeared more adept at differentiating infant leg movements from background movement. Unconstrained infant movements produced rates of rotation of 300-900 degrees/s, while constrained movements, such as those produced in a car seat, were represented by rates of rotation of 30-200 degrees/s.

Results: Preliminary analysis shows that gyroscope data are better than acceleration data for differentiating infant leg movements by age and context and for discriminating extraneous background movement. Peak rotational kicking rate, as measured by the gyroscopes, increased with infants' age.

Conclusion: It is feasible to collect full-day movement monitoring across the first year of life with sensors attached to infants' legs. We will validate the sensor data, relate leg movement trajectories to developmental milestones, and expand to assess infants with neurodevelopmental disorders.

Poster #3

Quantifying the feasibility of pairing tDCS with standard physical therapy following neurological insult using clinical and robotic assessment tools

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Introduction: Following neurologic insult, an imbalance between the affected and unaffected cortical hemispheres may contribute to functional impairments. Bihemispheric transcranial direct current stimulation (tDCS) may help diminish this imbalance.

Purpose: We examined the feasibility of pairing bihemispheric tDCS with standard upper extremity physical therapy (UE-PT) in individuals with chronic stroke and TBI.

Methods: Five individuals with chronic stroke, one individual with TBI, and one individual with stroke resulting from TBI participated in 24 sessions of UE-PT (40 minutes, 3 times/ week). Bihemispheric tDCS at 1.5mA was delivered over motor cortex during the first 15 minutes of UE-PT. Outcomes were assessed using clinical (UE Fugl-Meyer, Purdue Peg Board, Box and Block, Stroke Impact Scale) and robotic (position sense, visuomotor control, executive function) assessments at 8 time points (2 pre-intervention, 2 interim, 1 post-intervention, 3 follow-up).

Results: Two participants with stroke did not complete the study. Of the remaining three participants with stroke, one exhibited significant improvements in robotic measures of visuomotor control, and two did not show significant recovery. The participant with TBI demonstrated improved visuomotor control and the participant with stroke resulting from TBI demonstrated improvements on the UE Fugl-Meyer and robotic measures of visuomotor control. The three participants with significant recovery maintained their improvements at follow-up. **Conclusions:** Our results show that bihemispheric tDCS may be a feasible, effective adjunct to UE-PT for providing sustainable improvement of upper extremity function. Robotic assessment may improve our ability to monitor longitudinal recovery in individuals who respond to treatment.

Poster #4

Activity-dependent mechanisms of neural circuit plasticity during limb-overuse following ischemic stroke

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Stroke is the number one cause of adult disability in the United States, but there are no current medical treatments. Previously published work in the lab identified a molecular growth program that is triggered in the peri-infarct cortex after stroke, a process that promotes axonal sprouting in the surviving brain. The current studies indicate new neuronal connections form after stroke in an activity-dependent manner. This finding is especially germane in light of the 2006 EXCITE clinical trial, which found that stroke patients who engage in constraint-induced movement therapy demonstrate significant and lasting motor improvements. We have developed a novel limb-overuse paradigm that is analogous to human constraint-induced movement therapy. Using this model, we hypothesize that a specific ensemble of genes drives circuit rewiring during post-stroke limb overuse, a clinically relevant rehabilitative therapy that converges injury and activity-dependent molecular processes.

Preliminary neuronal tracing data suggest that recovery from forelimb motor stroke involves the formation of new circuits between the premotor areas and cortical areas located posterior and medial to the caudal forelimb region, including trunk motor areas and retrosplenial cortex. The cells that comprise these stroke-repair circuits have been labeled with a fluorescent neuronal tracer, specifically isolated by FACS, and are undergoing RNA-sequencing to generate an "activity-dependent transcriptome." In parallel ongoing studies, a number of stroke-induced and activity-regulated candidate gene systems are being screened in-vitro for potential roles in axonal sprouting. Selected candidates that increase neuronal sprouting will advance to in-vivo genetic manipulation within the premotor circuits mapped during post-stroke limb-overuse.

Poster #5

Frontal-Subcortical Function and Use of Assistive Speech Devices for Aphasia

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Assistive speech devices (ASDs) may augment communication efficacy in aphasia. However, patients may have difficulty using a mobile device, which requires diverse mental abilities including cognitive motor planning, concentration and sequencing. We wished to evaluate whether performance on specific neuropsychological tests could predict device use success. 20 people with aphasia (60.6±14.3years) completed 9 tasks, including Finger Tapping Test(FTT), aphasia-adapted Frontal Assessment Battery(FAB), Test of Oral and Limb Apraxia(TOLA), Western Aphasia Battery(WAB), Behavioral Inattention Test(BIT), Communicative Effectiveness Index(CETI), Catherine Bergego Scale(CBS), Naturalistic Action Test(NAT), and Neuropsychological Assessment Battery(NAB). All patients were trained to use an ASD (O'Brien Technologies Survivor Speech Companion System) followed by 7 days' unrestricted home use. Then, each participant completed 3 device-based communication tasks (tell marital status, give directions to Kessler Foundation, and ask for water). We performed a Stepwise Discriminant Function Analysis to evaluate how pre-trial tests performed in grouping High(>80%) vs. Low(<80%) scorers. FAB was the only significant predictor of device use success (Wilk'sLambda=0.713,F=6.856,p=0.018,28.7%variance), correctly classifying 80% of High/Low scores. A Factor Analysis indicated that a factor including FAB, WAB, BIT, NAB and TOLA explained 45% of variance (eigenvalues>1). Identifying people with aphasia who can benefit from an assistive speech device is vital to prescribing an ASD. Here, aphasia severity was *not* predictive, but an aphasia-adapted version of the FAB predicted device use success. These results show that frontal cognitive assessment may be needed in standard ASD assessment. Further research to identify the relation between skills assessed by FAB and neuropsychological deficits in aphasia is indicated.

Poster #6

Potential therapeutic effects of sensory tongue stimulation combined with task-specific therapy in people with spinal cord injury

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Background: Sensory stimulation combined with training has been shown to enhance motor recovery in people with neurological injuries. Sensory tongue stimulation is thought to activate regions of the brainstem important for balance and gait. The aim of this case report was to evaluate the feasibility and potential benefits of a gait and balance training program combined with sensory tongue stimulation in people with incomplete spinal cord injury (iSCI).

Methods: Two male participants (S1 and S2) with chronic motor iSCI completed 12 weeks of balance and gait training combined with sensory tongue stimulation using the Portable Neuromodulation Stimulator (PoNS). Laboratory based training involved 20 minutes of standing balance with eyes closed and 30 minutes of body-weight support treadmill walking. Home based sessions consisted of balancing with eyes open and walking with parallel bars or a walker for up to 20 minutes each. Subjects continued daily at-home training for an additional 12 weeks as follow-up.

Results: Both subjects were able to complete a minimum of 83% of the training sessions. Standing balance with eyes closed increased from 0.2 to 4.0 minutes and 0.0 to 0.2 minutes for S1 and S2, respectively. Over ground walking speed improved by 0.14 m/s for S1 and 0.07 m/s for S2, and skilled walking function improved by 60% and 21% for S1 and S2, respectively.

Conclusions: Sensory tongue stimulation combined with task-specific training may be a feasible method for improving balance and gait in people with iSCI. Our findings warrant further controlled studies to determine the benefits of this program.

Poster #7

Does paired stimulation of cutaneous and proprioceptive receptors enhance motor performance of a skilled walking task?

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Background: Many people with a spinal cord injury who have recovered some basic walking ability still have problems with performing more skilled walking tasks, such as stairs and obstacles. There is increasing evidence that poor utilization of afferent feedback pathways from sensory receptors contributes to disordered movements during walking. Sensory inputs from cutaneous and proprioceptive receptors play important roles in locomotor control and motor learning. Advanced locomotor rehabilitation technology provides an opportunity to investigate strategies to enhance activation of sensory pathways along with task-specific training to facilitate recovery of walking function. The purpose of this study is to compare the effects of paired and unpaired stimulation of cutaneous and proprioceptive receptors on the performance of a skilled walking task in able-bodied adults.

Methods: Subjects performed a skilled walking task focused on foot height with the Lokomat robotic-gait orthosis. They were presented with real-time visual feedback of their foot height along with a virtual target that they were instructed to match during the swing phase. The target height changed randomly with each of the 30 steps during the pre- and post-training tests. For the training bout, subjects were randomized to receive one of 4 different practice conditions: 1) no sensory stimulation, 2) proprioceptive only, 3) cutaneous only and 4) paired proprioceptive and cutaneous. Cutaneous stimulation was applied by electrical stimulation to the sural nerve at 1.5 times perceptual threshold. Proprioceptive stimulation was delivered as a Lokomat-applied resistance against hip and knee flexion during swing. Foot trajectory error was measured as the vertical distance between the target and actual foot height.

Results: During the pre-training trial, the average error was 43.1 mm (SD: 13.1 mm). During training, subjects showed improvements in the task performance, as exemplified by a decreasing trend in error over the duration of training (approximately 200 steps). Following training, the average post-training test error improved by 6.2 mm and 3.1 mm for the proprioceptive only and paired stimulation conditions, respectively. Further data collection is warranted to confirm the benefits of enhanced sensory stimulation on skilled locomotor performance.

Discussion: Preliminary findings indicate that performance of a challenging motor task can improve after short-term training with enhanced sensory stimulation. Robotic-based training offers a unique method to target specific features of walking that are important for adapting the locomotor pattern to perform everyday tasks.

Poster #8

A novel approach to quantifying changes in locomotor EMG patterns in incomplete spinal cord injury

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In incomplete spinal cord injury it has been shown that robotic assisted body weight supported treadmill training can improve stepping. Presumably, this is in part due to improving muscle activation patterns. Methods to quantify those patterns, their degree of abnormality and their change over time have been an area of ongoing research. The goal of this project was to determine the normalcy of the SCI motor patterns by first developing a prototypical motor pattern for the uninjured population and then comparing the SCI motor patterns to this prototype before and over the course of locomotor training. To develop the prototypical muscle activation pattern, electromyography (EMG) from the right and left quadriceps, hamstrings, tibialis anterior and soleus muscles were collected from 10 neurologically intact individuals while stepping in the Lokomat (for comparison to SCI). These muscle activation patterns were studied under various combinations of loading (40, 60, 95% body weight support; BWS) and treadmill speed (0.5, 0.7, 0.9 m/s). The EMG patterns for each gait cycle were divided into 10 equal bins and averaged within subjects over at least 15 steps. Within a subject, the average EMG amplitude for each muscle within a bin was used to create a vector such that each muscle made an equal contribution it value. The vector was then normalized to the magnitude of the vector thus creating a response vector. The response vectors (i.e. the relative activation of each of the 8 muscles in one bin) for each bin were then averaged across subjects to create the prototype pattern. For the injury group, EMG from 4 subjects with incomplete SCI were recorded at 2 speeds (0.5 & 0.7 m/s) and 2 loads (40 & 60% BWS) while stepping in the Lokomat. EMG patterns were binned and compared to the uninjured prototype pattern using a similarity index (i.e. the cosine of the angle between prototype vector and individual SCI subject's vector). The results for the uninjured subjects indicated that the lowest BWS conditions (40 & 60% BWS) produce similar EMG patterns across uninjured individuals whereas the highest BWS (95% BWS) produce atypical motor patterns. For the SCI group, initial results indicate that the similarity index can differentiate between muscle weakness (where muscles activate appropriately but with low magnitude) and abnormal muscle activation patterns (i.e. increased dysynergias). Currently, the similarity index is being used to tract changes in stepping EMG patterns in individuals with SCI related to locomotor training and transcutaneous spinal cord stimulation. In the future this approach may be used as a metric to characterize injury profile and guide therapy.

Poster #9

Measurement of volitional muscle activity initiation and cessation after spinal cord injury

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Following spinal cord injury (SCI), control over muscle activation and relaxation is usually impaired leading to slowed movement and hypertonia. Most efforts to date have measured and described impairment of the ability to activate paralyzed and/or paretic muscles. Equally important to restoring motor control, however, is the ability to deactivate muscles that have been inappropriately recruited or to accurately end contraction at the conclusion of a voluntary task or movement. Surface electromyographic (sEMG) recordings were made in 11 non-injured and 10 incomplete SCI subjects while attempting volitional ankle dorsiflexion in response to a 5-second audible cue. They were instructed to perform voluntary ankle dorsiflexion as quickly as possible upon hearing the cuing tone and then to relax as completely and quickly as possible when it ended. sEMG from the tibialis anterior (TA) and triceps surae (TS) muscles was recorded with a 2 KHz sampling rate and processed into RMS envelopes with a 20Hz smoothing filter. The TA envelope provided measurement of time from the cue to sEMG onset and to peak amplitude along with the time from cue cessation and beginning of RMS amplitude decline to the end of muscle activity. The antagonist envelope, from the TS, provided measurement of the time after cue cessation and the amplitude and duration of an antagonistic burst of muscle activation. No difference was seen between the two groups for the time to first motor unit fired, which is cognitive reaction time. From the first unit fired to peak firing, non-injured subjects recruited TA motor units more quickly than did SCI subjects, 245 ± 66 ms and 974 ± 674 ms respectively. Cessation of firing was also faster in the non-injured group with the time from beginning of firing decrease to the end of motor unit firing taking 399 ± 202 ms, whereas SCI group cessation required 544 ± 343 ms. Finally, 86 % of trials in non-injured subjects included a burst of antagonist muscle firing with a mean peak RMS amplitude of 36 ± 23 μV and duration of 237 ± 149 ms that was seen in only one subject in the SCI group. These results suggest that reduced supraspinal control over motor unit firing in SCI impacts both the initiation and cessation of contractions that can be quantified using the measurement techniques presented. Further, it suggests that there are at least two functional mechanisms for normally ending a volitional contraction, cessation of descending excitation of the agonist and transient excitation of antagonistic muscle motor units. Both of these seem to be altered by SCI and may explain abnormalities of muscle relaxation.

Poster #10

Acute and post-acute assessment of postural control and cognitive efficiency following concussion.

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Background: After concussion, individuals are frequently affected by changes in postural control and cognitive functioning. We recently reported postural control deficits in a group of athletes with prolonged recovery from concussion. However, findings from this subset with known and persisting balance problems may not accurately reflect postural control among the larger population of athletes who have sustained concussion.

Objective: To determine: 1.) if impaired postural control was detectable in the acute and post-acute period after concussion, 2.) the timeframe of recovery of postural control and 3.) if recovery timeframe for postural control was similar to that of cognition.

Setting: This study was conducted at Oregon Health & Science University, Portland State University, and Lewis & Clark College.

Participants: Eleven athletes (age 20±1; 9 men, 2 women) who had sustained sports-related concussion and 17 age-matched students athletes with no history of concussion participated in the study.

Design: After concussion, participants were serially tested on postural control at approximately days 2, 5, 9, and 14. Cognition was assessed at baseline (pre-season) and approximately days 2, 5, and 9.

Outcome measures: Two-dimensional sway area during the Instrumented Balance Error Scoring Scale (IBESS) test from one inertial sensor on the belt. Sway area was averaged over three 20-second trials (feet together, single limb stance and tandem on firm surface; eyes closed). Cognition was estimated using the ImPACT screening tool (preliminary data are based on the Cognitive Efficiency Index).

Results: The IBESS revealed differences ($p= 0.047$) in postural control between acutely concussed (2 days post-injury) and controls. At 2 days post-injury, our case group was divided between those with normal (54%) and abnormal (45%) balance. Preliminary results indicated that 40% remained abnormal 9 days after injury, 20% at 16 days and 1 person at day 23. Of note, at day 5, 80% of the athletes with abnormal balance had returned to baseline cognitive efficiency and were returned to play.

Cognitive recovery post-injury was not consistently associated with balance scores. The Cognitive Efficiency Index from ImPACT did not correlate with balance measures at any of the post-injury measurement times (Day 2: $r=0.09$; p 0.79; Day 5: r-0.45, $p=0.19$ and Day 9 $r= 0.10$, $p=0.78$).

Conclusions: Athletes with abnormal postural control and prolonged return to normal balance had minimal overlap with the individuals who had prolonged return to cognitive baseline measure. Different neural pathways may recover at different rates after concussion warranting objective evaluation of both domains in clinical assessment.

Poster #11

A quantitative method for measuring bilateral arm activity via accelerometry

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***Background*.** Neurological injury (e.g. stroke) commonly results in motor deficits, such as hemiparesis. Recovery of bilateral arm function is important for the performance of many everyday tasks. Some assessments measure bilateral arm function inside the clinic, but do not assess real-world function. Additionally, existing assessments do not quantify the contribution of each arm to activity. If the goal of rehabilitation is functional restoration of the impaired arm, then this is an important construct to measure.

Objective. The purpose of this study is to examine the construct validity of a novel method for assessing bilateral arm activity during everyday tasks using wrist-worn accelerometers.

Methods. Neurologically intact adults (N = 74) wore accelerometers on both wrists while completing 10 everyday, unilateral and bilateral tasks (e.g. typing, writing, cutting, folding towels, stacking boxes). For each task, the magnitude of acceleration was determined for each arm, and also summed to determine the bilateral magnitude. The ratio of arm acceleration (magnitude ratio) in one arm vs. the other was calculated, such that values close to 0 indicate unilateral activity and values close to 1 indicate equal contributions from each side. Time spent in bilateral activity (i.e. simultaneous arm movement) was calculated, and estimated energy expenditure (as measured by MET values) was also determined.

Results. Bilateral magnitude varied, with some tasks completed with low bilateral magnitudes (e.g. writing), some with high bilateral magnitudes (e.g. stacking boxes), and others with variable bilateral magnitudes (e.g. grooming). Only a few tasks were truly unilateral, as most magnitude ratios were greater than 0. There was considerable variability across tasks and across individuals. Time spent in bilateral activity and the magnitude ratio were strongly correlated ($r = 0.93$, $p < 0.01$). Energy expenditure and bilateral magnitude were also strongly correlated ($r = 0.74$, $p = 0.02$).

Conclusions. During everyday activities, the contribution to bilateral activity from each arm varies across tasks and individuals. These results demonstrate construct validity of this assessment method for quantifying bilateral arm activity, and can now be used to assess recovery of real-world, bilateral arm function in patient populations.

Poster #12

Spatial cognitive function of the right insula: A study with stroke survivors

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Brain lesions involving the right insular cortex may induce spatial neglect, a neurocognitive disorder manifested as a failure to attend or act upon stimuli on the contralesional (i.e., left) hemispace. To investigate specific functional deficits following insular lesions, we studied individuals with lesions centered at the right insular region and examined whether an insular damage critically predicts impairment in a specific everyday activity. 12 participants (6 men & 6 women; mean age = 72.3, SD = 10.9) were included for their lesions restricted in the right insular region; with more than 90% of the insular cortex and less than 10% of the surrounding areas. All the participants met the criterion of having spatial neglect, assessed with a neuropsychological test, the Behavioral Inattention Test (BIT) using the standard cutoff score of 129/146; having mean BIT score = 95.2, SD = 44.3. Participants' performance of everyday activities was evaluated with the Functional Independence Measure (FIM) and the Catherine Bergego Scale (CBS). With 18 evaluation items (score = 1-7 per item, higher value = better function), FIM is the most common clinical measure for independence following stroke. The 10-item CBS (score = 0-3 per item, higher value = greater severity) is an observational assessment for spatially asymmetrical action deficits in daily life. Participants' clinical brain images were acquired on average 4.8 days (SD = 7.9) post stroke, and their behavioral performance was evaluated 18.6 days (SD = 7.4) post stroke. Overall, participants had difficulty performing everyday activities, indicated by their total FIM (mean = 102.4, SD = 30.0) and CBS scores (mean = 15.7, SD = 6.9). To investigate whether a lesion location in and around the right insula was critically associated with a specific FIM or CBS item; we performed a series of voxel-based lesion-behavior mapping analysis with 5% false detection rate. The only result that reached statistical significance was from a CBS item for evaluating difficulties in finding personal belongings in a familiar environment. The critical region (z = 2.826 - 3.891) was at the anterior insula with its adjacent extreme capsule and inferior medial temporal areas. This finding suggests the function of the anterior insula in visual search or mental representation of familiar objects in the context of a familiar environment.

Poster #13

AMES + brain stimulation for treatment of hand plegia: A proof-of-concept study

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It has been estimated that half of all stroke survivors never regain functional use of the upper limb (UL). We investigated, in a pilot study with 6 participants (average age = 54 yr; average time since stroke = 39 months), the effects of AMES (i.e., assisted movement with enhanced sensation) treatment with concurrent brain stimulation. Inclusion criteria included >1 yr post-injury, ≤3 score on modified Ashworth scale; no measurable extension of the thumb, fingers or wrist, but with some residual proprioception in the affected UL. The Study Physician screened out study candidates with co-morbidities that would interfere with full study compliance. Upon enrollment, each participant was randomized to one of 2 treatment groups, one, in which AMES was combined with tDCS, and the other, in which AMES was combined with rTMS. There was no control group in this study.

The participants were treated for 20 min during each of 30 sessions, typically conducted 3 times per week over a period of 10-12 weeks. On each treatment day, the participant sat with the affected UL in the AMES device while being prepared for either tDCS or rTMS stimulation. Both methods of brain stimulation were intended to stimulate the motor cortex on the injured side of the brain. During AMES treatment, the AMES robotic device ranged the thumb and 4 fingers at the MCP joints (±15 deg, 5 deg/s), opening and closing the hand. During hand-opening, a muscle vibrator stimulated (60 pulses/s, 2 mm) the long flexor tendons of the thumb and fingers; during hand-closing, a different vibrator stimulated the corresponding extensors. The participant faced a computer screen that provided real-time EMG biofeedback from the finger flexor and extensor muscles. The participant was instructed to assist the movement imposed on the hand by increasing the agonist EMG to a target level while minimizing the antagonist active. The target EMG was initially set, and then maintained, at a level of 25% of the participant's maximum volitional agonist EMG.

All 6 participants regained some volitional movement at one or more of 6 locations: thumb, fingers (n=4), and wrist, at some point during the 10-12 week treatment period. On average, participants exhibited some volitional extension on 13/30 treatment days, and on each day with volitional movement, it observed at an average of 1.9 of the 6 possible locations. Scores improved slightly on the Chedoke-McMaster Assessment, but not significantly. Similarly, a strength test showed no significant strength gains. However, one participant recovered considerable functional use of the affected hand, and this recovery has persisted for 1-1/2 years post participation. These results demonstrate the feasibility of conducting a clinical trial, without significant risk to participants, and further suggest some potential to reverse chronic hand plegia after stroke.

Poster #14

Reorganization of the locomotor network in Parkinson patients with freezing of gait

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Freezing of gait (FoG) is a unique and disabling clinical phenomenon of advanced Parkinson's disease (PD) characterized by brief episodes of inability to step that often occurs on initiation of gait. Recent work implicates compromised structural integrity and transient functional disconnection between subcortical and cortical regions of the locomotor network in individuals who experience FoG. In the current study we use a novel multimodal neuroimaging approach to assess differences in functional and structural connectivity of the locomotor network between PD patients with (FoG+) and without (FoG-) freezing of gait along with age-matched controls.

Fifteen mild to moderate patients with PD and fourteen age-matched healthy controls (HC) were recruited for the current study. Parkinson's patients were tested in the morning off medication and were classified as either FoG+ (n = 8) or FOG- (n = 7) based on their new freezing of gait questionnaire score (NFOGQ). Resting state functional MRI were collected and functional connectivity of the locomotor network was assessed between seed regions of the supplementary motor area (SMA) and bilateral subthalamic nuclei (STN) and cerebellar and mesencephalic locomotor regions (CLR and MLR, respectively). Diffusion weighted images were also collected and probabilistic tractography was performed between locomotor hubs where functional connectivity differences were observed and there are known anatomical connections. Finally, clinical testing to assess disease severity and gait function was performed.

Principal results include FoG+ patients showed greater connectivity between bilateral MLR and SMA ($P < 0.02$) and between left CLR and the SMA compared to both FoG- and HC ($P < 0.03$). We report a striking difference in the relationship between structural and functional connectivity between the right MLR and SMA, whereby more structural connections were associated with *reduced* functional communication in HC ($r = -0.37$), but *increased* functional communication in FoG+ ($r = 0.50$). Additionally, more functional connectivity between the right MLR and SMA was strongly correlated with both clinical ratings of FoG ($r = 0.71$) and self-reported NFOGQ scores ($r = 0.74$) in FoG+, suggesting that the observed increases in communication are not compensatory.

The current findings demonstrate a re-organization of functional communication within the locomotor network in FoG+ patients whereby the higher order motor cortices responsible for gait initiation communicate with the MLR and CLR to a greater extent than the patterns observed in FoG- and HC. The observed pattern of altered connectivity in FoG+ does not appear to serve a compensatory role as evidenced by the positive association between ratings of FoG and increased functional connectivity in the MLR - SMA loop. Intervention tasks targeted at reducing communication in the disadvantageous locomotor loops identified here (MLR/CLR - SMA) may result in improved gait initiation and a reduction in freezing.

Poster #15

Targeted exercises to increase cortical influence over spinal reflexes

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Background: Spinal contusions tend to spare a portion of neural circuitry. Spared circuits consist predominantly of reflexive brainstem- and spinal-origin tracts rather than volitional corticospinal fibers. To improve volitional control of muscles **below** spinal injuries, cortical connections to spared brainstem circuits must be strengthened **above** spinal injuries. We hypothesize that through Hebbian mechanisms, repetitive co-activation of cortical and brainstem circuits will strengthen detour pathways for cortical signals to travel **around** spinal lesions.

Objective: To use targeted exercises to demonstrate the utility of strengthening cortical influence over spinal reflexes.

Methods: In this pilot study, uninjured volunteers underwent one session each of three different types of exercise: (1) treadmill walking, (2) balance platform exercise, or (3) balance exercise combined with skilled hand activities (multimodal exercise). Electrophysiological outcome measures were recorded immediately before and after each exercise session. The primary outcome is the magnitude of soleus H-reflex facilitation by subthreshold transcranial magnetic stimulation (TMS). H-reflex facilitation occurs during two peak time windows relative to TMS – an “early” (<20 ms) window thought to represent *direct* corticospinal facilitation, and a “late” (60-80 ms) window thought to represent *indirect* facilitation, partly through corticobulbar connections. Other outcomes include soleus H/M ratio (an electrophysiological proxy for spasticity), central motor conduction time (a marker for speed of transmission between the cortex and spinal cord), and motor evoked potential amplitudes.

Results: Preliminary results, based on enrollment of 18 out of 24 planned participants, show post-exercise H-reflex facilitation in the late time window of 136.1±9.0%, 129.8±7.8%, and 117.7±4.5% after balance training, multimodal training, and treadmill training, respectively. In the early time window, post-exercise H-reflex facilitation is 128.3±9.2%, 121.5±5.6%, and 109.2±2.0% after balance, multimodal, and treadmill training, respectively. The ratio of maximal H/M amplitude decreased by 17.2±6.1%, 14.3±7.1%, and 6.2±10.3% after multimodal, balance, and treadmill training, respectively. Furthermore, central motor conduction time decreased by 0.83±0.44 ms and 0.63±0.32 ms after multimodal and balance training, respectively, whereas it increased 0.18±0.36 ms after treadmill training.

Conclusions: Balance training may increase supraspinal influence over spinal reflexes in the legs. While this pilot study in uninjured individuals continues, we have begun to incorporate a similar training and measurement approach into a clinical trial to test the effects of treadmill versus multimodal exercise in individuals with chronic spinal injury.

Poster #16

Damage and recovery following white matter stroke: a key role for age

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Subcortical white matter stroke (WMS) constitutes up to 30% of all stroke subtypes and has devastating clinical consequences. Mechanisms of damage and repair in WMS mainly involve oligodendrocyte and axon injury and regeneration, and are distinctly different from the cellular and molecular events resulting from large artery, "gray matter" stroke. Diminished recovery from stroke in aged patients implies that damage and repair processes are affected by advanced age, but such effects have not been studied in WMS. This study aimed to evaluate the effect of age on white matter damage and repair using a WMS mouse model, and promote functional recovery in aged animals following this type of stroke. WMS was produced with focal microinjection of the vasoconstrictor L-NIO into the subcortical white matter ventral to the mouse forelimb motor cortex in young adult (2 months), middle aged (15 months) and aged mice (24 months). A blocker of the neural growth inhibitor Nogo, NgR^{OMNI}, was administered to aged mice following stroke to promote repair in a systemic delivery approach designed to model what would be practical in humans. Functional impairment and recovery were assessed using the pasta matrix reaching task, a behavioral test aimed at evaluating strength, reach capacity and dexterity of the mouse forelimb, as well as the grid walking task. WMS was found to produce inflammation, localized oligodendrocyte cell death and white matter atrophy that were more pronounced in aged animals compared to young adults. Behavioral testing revealed an age-dependent exacerbation of forelimb motor deficits caused by the stroke, with decreased long-term functional recovery in aged animals. Treatment with NgR^{OMNI} resulted in gradual behavioral improvement in aged mice, and a return to control levels one month after WMS -- a similar recovery profile to that observed in untreated young-adult mice. These findings demonstrate a profound effect of age on the outcome of WMS, but suggest that targeted therapeutic interventions can effectively restore function in aged animals.

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Poster #17

Feasibility of Bilateral Arm Training in the Subacute Setting

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Purpose: Of the approximately 800,000 stroke survivors per year, well over half are left with significant residual disability and 95% residual arm dysfunction. Effective strategies are needed to reduce the long-term disability from upper extremity (UE) hemiparesis. We have shown that six weeks of repetitive non-progressive bilateral arm training with rhythmic auditory cuing (BATRAC) improves UE motor function in mild and moderately-affected patients well beyond the three-month period. It has not yet been investigated if use of this training would be beneficial in the subacute stage where most recovery takes place and the potential for functional gain may be greater. The purpose of this study was to examine the feasibility of BATRAC training in the subacute setting and to compare the functional outcomes from adding BATRAC training versus additional time-matched standard of care (SOC) training to current SOC upper extremity retraining.

Subjects: 13 patients 2 - 12 weeks status post first-time stroke, receiving outpatient therapy at a subacute facility**.**

Methods: Patients received either 18 sessions of BATRAC training (n=8), or 18 sessions of time-matched SOC upper-extremity training in addition to SOC (n=5). BATRAC training included 4 five-minute sessions of repetitive bilateral reach and return movements over 40-minutes time. Additional SOC training was not prescribed but recorded. Therapists were asked to provide approximately 20 minutes active engagement in "more of what they offered in SOC" over a 40-minute treatment window. Progression of training was recorded for both groups. Primary outcome measures included Wolf Motor Function Test (WMFT), Fugl-Meyer Upper Extremity Test (FM), and the University of Maryland Arm Questionnaire for Stroke (UMAQS). Training was completed by therapists within the subacute facility. Testers from the research lab, who were blinded to group, completed tests in the subacute facility.

Results: Both groups demonstrated significant gains ($p<.05$) in the FM and UMAQS, with a larger effect seen in the BATRAC group. Only the BATRAC training group improved in the WMFT test (timed tasks). Review of differences between the two training approaches demonstrated a higher number of repetitions of movement practice for the BATRAC training group. BATRAC training focused on bilateral active-movement practice compared to SOC that focused on predominately unilateral UE movement of paretic limb or compensatory task practice with the nonparetic limb. SOC progressions did not include increases in speed but increases in types of activities trained compared to BATRAC training which focused on one reach and return movement with progression of speed and extent of movement.

Conclusion: We have demonstrated the feasibility of BATRAC training in the subacute setting with tolerance to progression. While additional BATRAC training was not definitively more effective than additional SOC training, features of BATRAC training such as repetition of movement practice and progression, including speed of movement, may be important considerations to improve upper extremity rehabilitation outcomes.

Poster #18

Bilateral reach training following a unilateral ischemic injury to the caudal forelimb area (CFA) of motor cortex in rats

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We have previously found that, following a unilateral ischemic injury to the caudal forelimb area (CFA) of motor cortex in rats, skill learning with the paretic limb or alternating skill training between the paretic and non-paretic limb facilitates paretic forelimb recovery in rats. Similarly, clinical literature indicates that rehabilitative training with only the paretic arm and both the paretic and non-paretic arm in individuals affected by upper extremity paresis is affective in restoring some function in the affected body side. Currently, no behavioral metric exists for rodents requiring use of both limbs concurrently as a rehabilitative training paradigm following unilateral focal motor cortical ischemic damage. In this study we sought to 1) develop a behavioral metric for bilateral rehabilitative training in a rodent model of focal motor cortical ischemia and 2) determine whether this behavioral metric benefits recovery in the paretic limb of rats compared to rats receiving either control procedures or rats receiving paretic limb training in a task that requires less skill. Animals were trained pre-operatively on a unilateral reaching task (single pellet retrieval task) and were then given an ischemic injury. Animals were then trained for 33 days on either 1), the bilateral reaching task, 2), a unilateral reaching task (tray task), or 3), control procedures. The rats were probed weekly using the single pellet retrieval task. The initial findings of this study indicate that skillful concurrent use of both forelimbs facilitates paretic forelimb recovery better than control procedures and as well as a skillful task requiring the use of only the paretic forelimb. Ongoing studies are examining the link between cortical reorganization and the behavioral effects of uni- versus bilateral training.

Poster #19

Impact of motor cortical stimulation timing during planar robotic training on neuroplasticity in older adults.

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Robotic technology is increasingly used for rehabilitation and the potential exists to enhance use-dependent plasticity with non-invasive motor cortex stimulation specifically timed with the practiced reaching movements. The objective was to determine how the timing of stimulation influenced neuroplasticity associated with robotic reaching. Sixteen participants completed 3 separate sessions with different stimulation timings (pre-movement, EMG triggered, random) during a repetitive reaching intervention using a planar robot with 480 trials of movement. Sub-threshold, single-pulse transcranial magnetic stimulation (TMS) was delivered at: pre-movement - 120-150ms prior to movement onset; EMG triggered - when muscle activity exceeded threshold; or randomly - anytime between visual cue and movement completion. Five assessments included the amplitude and direction of TMS evoked movements with corresponding motor evoked potential (MEP) recordings from the biceps, triceps, anterior and posterior deltoid muscles. Each assessment included 10 averaged trials and MEP data were organized into elbow and shoulder agonist and antagonist groups. Change scores from the initial assessment were calculated as follows: % change in amplitude, absolute change in direction (0-180 degrees), and change in MEP amplitude. Data were analyzed using a general linear model with repeated measures for time and a between subjects effect for stimulation conditions. The evoked movements significantly increased in amplitude following the pre-movement and random conditions, but not following EMG triggered condition ($p < 0.05$). The TMS evoked directions significantly changed following all conditions ($p < 0.05$), and no differences between groups were observed. There was a significant difference between conditions for shoulder and elbow agonist MEPs with a general increase in amplitude following pre-movement and a significant decrease following the EMG triggered condition ($p < 0.05$). These findings demonstrated that stimulation delivered during pre-movement and EMG triggered conditions influenced neuroplasticity with a robotic reaching intervention, yet the mechanism by which these changes occurred appeared to differ. The direction of plasticity may change rapidly and selectively during the planning and production of movement. This dynamic change in plasticity shapes the way in which practice results in motor system changes.

Poster #20

Transcallosal effects of chronic below-elbow arm amputation: a pilot study

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Background: The large-scale cortical reorganization that occurs after limb or digit amputation is well known. However, most of what is known is limited to the primary motor cortex contralateral to the amputated limb ("affected" hemisphere), with little consideration of the possible effects of these changes on the other ("unaffected") hemisphere. Based on the known expansion and increased excitability of the representational areas of muscles proximal to the amputation and the strong transcallosal connections between homologous motor areas, we hypothesize that interhemispheric inhibition (IHI) from the affected to the unaffected hemisphere will be greater than that from the unaffected to affected hemisphere and greater than that observed in controls.

Methods: A convenience sample of 3 chronic (>1 yr) below-elbow amputees (age 33 ± 21 yrs) and a comparison group of healthy controls (age 31 ± 8 yrs) have been enrolled. To measure IHI, transcranial magnetic stimulation (TMS) was used to elicit an ipsilateral silent period. Since it is elicited during sustained muscle activation, the ipsilateral silent period is expressed as % inhibition during the silent period relative to the pre-stimulation muscle activation level. IHI of the biceps and triceps brachii primary motor cortex representations was measured from the affected to the unaffected hemisphere and vice versa, as well as in healthy controls.

Results: In the amputees, IHI from the affected to unaffected hemisphere biceps brachii representation averaged 47.5 ± 6.9%, compared to 29.8 ± 7.3% from the unaffected to affected hemisphere, and 27.6 ± 10.0% in controls. A similar pattern was observed in IHI of the triceps brachii: 36.2 ± 9.5% inhibition targeting the unaffected hemisphere, compared to 25.7 ± 9.7% targeting the affected hemisphere and 26.4 ± 10.0% in controls.

Discussion: This preliminary analysis suggests that below-elbow arm amputation can result in an imbalance in the strength of interhemispheric inhibition, such that the affected hemisphere inhibits the unaffected hemisphere more strongly than vice versa. Imbalances in excitability and inhibition between motor cortices can contribute to motor impairment. This imbalance may contribute to the intact arm motor deficits that have been reported in chronic amputees.

Poster #21

Graph Theoretical Analysis of Resting State EEG in Post-acute Stroke Recovery

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Purpose: Graph Theoretical Analysis (GTA) has emerged as an important methodology to further understand the complex network dynamics of the human brain. In this study we used GTA to characterize changes in brain electrical activity (EEG) during post-acute hospitalization after hemiparetic stroke. The aim was to characterize changes in cortical networks associated with early stages of motor recovery and underlying neural plasticity. Specifically GTA was applied to understand how the pre- post-modulations in resting brain networks of post-acute patients would relate to improvements in lower extremity (LE) motor control and walking function.

Subjects: Participants (n = 13) who were admitted to the inpatient stroke unit of a rehabilitation hospital for standard-of-care physical, occupational, and speech therapy provided informed consent as approved by the IRBs' of both the University of Maryland School of Medicine and the Baltimore VA Office of Research and Development.

Methods: Baseline tests included 64-channel EEG collected during seated conditions of eyes-open and eyes-closed, evaluation of paretic ankle motor control using an ankle robot, and overground walking on an 8m instrumented gait mat. Participants received usual daily therapies, plus an extra session of paretic ankle exercises, either by playing videogames on the ankle robot, or by receiving dose-matched manual stretching. Baseline tests were repeated one day prior to discharge. Pre-post comparisons were performed with paired t-tests, and linear regression was used to relate the changes in GTA-derived Small Worldness (SW) as a metric of global network efficiency to changes in selected motor variables.

Results: Patients entered the study 14.9±11.5 days after stroke. By the time of discharge overground gait speed increased two-fold ($p \le 0.01$). Paretic ankle motor control (peak and mean speed, both $p \le 0.05$) and several spatiotemporal gait parameters also improved (cadence, paretic-nonparetic step-time ratio, stride length and paretic single support, all $p \le 0.05$). The change in resting state alpha-band SW correlated significantly with the change in the peak dorsi-plantarflexion speed ($p \le 0.05$), suggesting that increases in SW were associated with improved paretic motor control. Similarly, there was a significant relationship between the increase in gamma-band SW and increased stride length during walking. These increases in SW suggest that early motor recovery involves complex reorganization of intracortical communications that are more efficient in support of LE function.

Conclusions: The use of GTA is feasible within the very early post-stroke period and may provide a sensitive set of measures to evaluate cortical interactions underlying motor learning and functional recovery. Future use of these methods may facilitate the design of more efficacious neurorehabilitation strategies that capitalize on early plasticity to enhance long term outcomes after stroke.

Poster #22

Reliability of Negative Bold in the Primary Motor Cortex

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For over ten years, the existence of the negative BOLD signal in fMRI has been demonstrated across multiple domains. There is strong evidence indicating that the negative BOLD response in the primary motor cortex represents an active inhibition of areas in which it is found. This has important implications for rehabilitation research as many disorders of the motor system are characterized by a loss of cortical inhibition otherwise found in healthy adults. This loss of inhibition is also seen during the aging process and is correlated with decreases in motor performance also associated with aging. The present study investigated the reliability of the evoked negative BOLD response in 7 healthy young adults during a finger tapping paradigm in fMRI over three sessions. The results are compared with a cohort of 7 healthy older adults agiain assessed over three imaging sessions. The findings indicate that negative BOLD can reliably be evoked in ipsilateral motor cortex across multiple sessions in younger adults. However, the spatial locus and magnitude of BOLD activity in ipsilateral primary motor cortex in older adults is greatly variable.

Poster #23

Mechanisms of rhythm and pattern generation of the human lumbar spinal cord tested by epidural stimulation

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The lumbar spinal cord has the capability to produce rhythmic motor outputs in the absence of descending modulations across mammals, including humans [1,2]. The human lumbar cord can generate a rich repertoire of rhythmic locomotor-like and non-locomotor like patterns in response to a non-patterned multi-segmental drive provided by epidural spinal cord stimulation (SCS) [2,3]. In the present work, we hypothesized that the variety of these rhythmic motor patterns can be explained by common basic control principles of central rhythm and pattern generation.

Ten motor-complete spinal cord injured subjects with epidural electrodes over the lumbar spinal cord for spasticity control were studied. SCS was applied in the supine position that reduced the influence of afferent information essential for rhythm generation (hip extension, limb load). Ten-second segments of stable rhythmic patterns of EMG activities in quadriceps, hamstrings, tibialis anterior, and triceps surae unilaterally were extracted from the EMG data. A non-negative matrix factorization (NMF) algorithm was applied to the pooled EMG profile-data across subjects, muscles and samples of stable EMG patterns to test whether decomposition would identify underlying basic activation patterns.

Thirty-nine samples of 10-second segments of rhythmic EMG patterns were identified in 7 subjects (effective SCS frequency: 29.5 ± 4.85 Hz). The rhythm frequency was identical across all muscles in a given sample. Despite the variety of rhythmic EMG patterns generated, NMF of the pooled data demonstrated that they could be closely reproduced by a linear combination of a small number of basic activation patterns with appropriate weights. According to the Akaike Information Criterion [4], a model with 3 basic activation patterns had the highest relative probability to best describe the EMG profile-data. Two basic activation patterns had sinusoidal-like shapes, one peaking during an extension-like and the other during a flexion-like phase. There was a highly significant negative correlation of their weights required to construct the various EMG profiles. The third basic pattern peaked in the early flexion phase and was not related to the other basic activation patterns.

The constant phase relation of rhythmic outputs to one lower limb suggests pluri-segmentally organized rhythm generation. The two elementary basic activation patterns closely resemble the two-phase motor pattern of fictive locomotion of experimentally reduced animal models that is generated by central pattern generating networks [1]. The third basic pattern confirms neural processes beyond half-center oscillations. Understanding the processing and pattern-shaping capabilities of the human lumbar cord networks is clinically significant for the modification of altered motor control in neurological conditions.

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Poster #24

Alternating reflex modulations by spinal neural circuits ‘outside' the human lumbar locomotor pattern generator

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Epidural lumbosacral spinal cord stimulation (SCS) generates a variety of motor outputs to the lower limbs of motor-complete spinal cord injured (SCI) individuals, depending on the applied stimulation parameters. Specifically, coordinated rhythmic flexion-extension movements can be evoked at 25-50 Hz [1]. The motor activities produced by SCS are comprised of series of stimulus-triggered posterior root-muscle (PRM) reflexes that are modulated to form the burst-like electromyographic (EMG) activities [2]. Periodic, alternating modulations of successive PRM reflexes are another consistent EMG pattern generated with SCS-frequencies and intensities below the ones leading to the rhythmic flexion-extension movements. These patterns, characterized by an oscillation period covering two consecutive responses and the attenuation of every other response magnitude, will be elaborated in the following.

PRM reflexes of quadriceps (Q), hamstrings (Ham), tibialis anterior (TA), and triceps surae (TS) bilaterally to SCS at 2-26 Hz derived from 8 motor-complete SCI individuals were analyzed for their EMG characteristics for 50 ms post-stimulus. Stimulation at 16 Hz and intensities of 1-1.5 times the respective motor thresholds was most effective to generate the alternating EMG patterns across all muscles, while there was no specifically effective segmental stimulation site. Generally, the alternating EMG patterns were established with the first few SCS pulses. Periodic reflex alternations occurred more frequently in the thigh (found in 29% of all data sets) than the leg muscles (20%). In-between Q and Ham, the EMG patterns were either modulated in-phase or had a reciprocal relation. In TA and TS, in-phase modulations of the EMG patterns in the antagonists were the common finding. In-between the left and right lower limb, series of PRM reflexes of a given muscle group were generally modulated in-phase.

The amplitude modulations of the successive PRM reflexes reflected the excitability of the spinal motor neural circuitry at the time each impulse arrived from the depolarized posterior-root fibers. The short period of SCS required to establish the alternating reflex modulations along with the lower effective SCS-frequencies and intensities as compared to those generating the rhythmic flexion-extension movements suggest the activity of relatively simple neuronal networks as the underlying mechanism. These networks may incorporate time-dependent processes that enhance or reduce neuronal activities and may include recurrent inhibition and reciprocal interconnection in-between circuits controlling different motor pools. Gaining insight into spinal mechanisms of inhibition and excitation as well as the frequency-specificity of their engagement in the processing of afferent volleys will be crucial for advancing and developing novel rehabilitation strategies.

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Poster #25

Educate, Train, Treat, Track: Bringing state of the art care to our Military with TBI

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A poster describing the U.S. Army Traumatic Brain Injury (TBI) program. Displays progress from the U.S. Army TBI Task Force. Also includes capabilities and services in the deployed and garrison environments within the context of Department of Defense (DoD) policy for TBI care and existing gaps within the system. Shows the evolution of, and current, policies and clinical algorithms in the deployed and garrison environments as well as DoD clinical recommendations. Poster includes the Neurocognitive Assessment Tool and role of neurocognitive assessment in return to duty decision making. Presents the DoD TBI coding procedures and discuss challenges in analyzing coded data. Shows Army TBI Research initiatives related to TBI Finally, displays the Army TBI education and training strategies used to educate a widely-dispersed population of medical staff and providers and specific tools and resources developed to support the TBI mission to include patient education handouts, educational videos and slide decks, and the TBI Rehabilitation ToolKit.

Poster #26

Premotor cortical stimulation in stroke rehabilitation: neural mechanisms of recovery

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In recent clinical trials, adjuvant cortical stimulation has shown no advantage in stroke rehabilitation, unlike in prior work. Variable success may be due to the fact that the usual target, the primary motor cortex (M1), is spared only in a few. Targeting higher motor areas, as premotor cortex (PMC), may be more effective as it assumes the role of damaged M1 and contributes more significantly to corticospinal and inter-hemispheric connections. Knowing individual mechanisms of recovery would help understand variability of effect. In a pilot randomized, double-blinded clinical study, we examine efficacy and underlying mechanisms of stimulating PMC in rehabilitation of hand in chronic stroke.
Patients were assigned to rehab+stim or rehab+sham groups. Rehabilitation was delivered for 1hr, 3 times/week for 5 weeks. Anodal transcranial direct current stimulation was applied at 1mA to PMC in stroke hemisphere using MRI-based stereotaxy. We measured impairments and force of paretic hand. Diffusion Tensor Imaging (DTI) defined integrity while Transcranial Magnetic Stimulation (TMS) noted physiologic efficiency of corticospinal tracts. TMS also noted transcallosal inhibition from stroke upon intact hemisphere. Functional Magnetic Resonance Imaging (fMRI) noted inter-hemispheric balance for M1 and PMC. Age-matched controls were also studied.
Impairments alleviated, while force of paretic hand improved across all patients; however, changes in only the rehab+stim group approached values in healthy. Rehab+stim group also improved corticospinal conduction, transcallosal inhibition exerted from stroke upon intact motor areas, and inter-hemispheric balance that shifted back to M1 and PMC in the stroke hemisphere. These mechanisms were less prominent in the rehab+sham group. Patients with greater integrity of corticospinal tracts from M1 and PMC in the stroke hemisphere and stronger changes in corticospinal conduction showed significantly better recovery of force of paretic hand [($r=.9$, $p=.01$; $r=.78$, $p=.05$) and ($r= .88$, $p= .02$)]. Those who showed greater shift of inter-hemispheric control to PMC in stroke hemisphere also exhibited higher recovery ($r=.79$, $p=.05$).
Thus, premotor cortex may be a potential surrogate target for stimulation in concurrent chronic stroke rehabilitation. Success of pairing may depend upon integrity and functionality of corticospinal output from primary and premotor areas and the potential of the targeted region (such as PMC) in stroke hemisphere to regain focus of movement control. Variability of adjuvant cortical stimulation in rehabilitation can be mitigated by addressing prognostic indicators with DTI, TMS and fMRI.

Poster #27

Diffusion Tensor Imaging exhibits more proximate and reliable Transcranial Magnetic Stimulation measures compared to fMRI in stroke

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In stroke, functional MRI (fMRI) serves as a poor guide to direct Transcranial Magnetic Stimulation (TMS). Localization with fMRI is variable since its hemodynamic contrast is contorted in and around infarcted tissue. Further, fMRI reflects activity in the grey matter, whereas TMS examines conduction via white matter, such as corticospinal tracts (CST). To develop a better guide for TMS in stroke, we examined whether imaging CST terminations in cortices using diffusion tensor imagining (DTI) is more reliable and proximate to sites of TMS than fMRI. Four patients with stroke and four aged-matched healthy controls underwent fMRI during hand movement, and DTI. Stereotactic TMS was delivered to motor cortical sites in a 7 X 5 grid in patients' affected hemispheres while we recorded 5 motor evoked potentials (MEPs) in the paretic first dorsal interosseous (FDI) muscle. We compared the distances between and reliability of MEPs at the following sites: site of highest fMRI activation, cortical sites with best myelin (transverse diffusion) and overall (fractional anisotropy) integrity of CST terminations, and optimal site of TMS (weighted center of gravity of MEPs). Overall, MEPs were reliable when TMS was applied to sites with best integrity of CST terminations; however, when TMS was applied to site of maximum fMRI activation, MEPs were absent in 50% patients and 25% controls. At sites of best myelin integrity of CST, trial-to-trial reliability of MEPs (measured with coefficient of variation) trended towards being better than that at site of maximum fMRI activation (55.58 ± 44.74% vs. 70.32 ± 13.63%) ($p = .07$). In the affected hemisphere, cortical site with best myelin integrity and overall integrity of CST terminations were closer to the optimal TMS site than site of maximum fMRI activation (4.1mm±5.0mm and 5.7mm±6.7mm vs. 14.9mm±3.9mm, respectively) ($p < .05$). Preliminary results of this ongoing work suggest that imaging corticospinal tracts may be reliable and accurate in localizing TMS in stroke. Future studies can explore whether DTI-guidance maximizes outcomes of therapeutic TMS in stroke rehabilitation. Exploring reliable navigation for TMS will allow us to customize therapy to the patient's own neural substrates.

Poster #28

Individually-Targeted Transcranial Direct Current Stimulation Enhances Fluency in Patients with Chronic Non-Fluent Aphasia

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Introduction: Emerging evidence suggests that transcranial direct current stimulation(tDCS) may improve naming in persons with chronic left hemisphere stroke and nonfluent aphasia. Language improvements beyond naming have not yet been thoroughly investigated. Moreover, different investigations have employed different electrode polarities (anodal or cathodal) at different sites (ipsilesional or contralesional cortex), raising the question of whether optimal stimulation parameters vary across aphasic subjects.

Methods & Procedures: Individuals with moderate to mild non-fluent aphasia have been recruited for this ongoing two-phase study. In Phase1, over the course of five non-consecutive days, participants underwent tDCS with four different stimulation montages (anode-F3, cathode-F3, anode-F4, cathode-F4) and a sham condition. Participants who demonstrated improvement in naming after stimulation with a specific electrode montage moved on to Phase2, a sham-controlled partial-crossover treatment trial employing the optimal stimulation montage identified in Phase1. Subjects in Phase2 completed three baseline behavioral sessions with the Western Aphasia Battery prior to treatment, and then received stimulation (20min,2.0mA,5x5cm electrode) for a total of 10days (Monday-Friday for two consecutive weeks).During stimulation, participants completed a constraint-induced picture-naming task, in which a barrier prevented the participant from viewing the experimenter. Subjects repeated the WAB two weeks, two months, and six months after treatment. Subjects in the sham arm received 10days of sham stimulation, and were tested at two weeks and two months, and then received real tDCS, with a two-week, two-month, and six-month follow-up. In addition to calculating the WAB aphasia quotient(WAB AQ; a composite assessment of speech production, comprehension, and repetition), the picture description component of the WAB was also scored using Quantitative Production Analysis(QPA), in order to further evaluate changes in language fluency across the categories of discourse productivity, sentence productivity, grammatical accuracy, and lexical selection.

Outcomes & Results: To date, 12 subjects have completed Phase1 of this ongoing investigation. Of these, 7 demonstrated statistically significant transient improvement in object naming ability following stimulation and were thus enrolled in Phase2. Optimal montage placement was highly variable across subjects. To date 5 of these subjects have completed a six-month follow-up. Compared to baseline, subjects showed significant improvement (paired-sample t-tests;$p<.05$) on the WAB AQ as well as measures of discourse productivity and grammatical accuracy at two weeks and two months following stimulation. Persistent improvement in the WAB AQ was also observed 6months following stimulation. The two subjects randomized to the initial sham treatment arm showed no significant change from baseline in post-sham testing.

Conclusion: The preliminary results of this ongoing investigation support prior work indicating that tDCS enhances recovery from chronic post-stroke aphasia. The results further suggest that in nonfluent patients tDCS may specifically enhance elements of fluency such as discourse productivity and grammatical accuracy. Finally, optimal electrode arrangement appears to vary across participants, suggesting that individualized treatment may further improve language outcomes.

Poster #29

Activation changes induced by mnemonic strategy training during memory encoding and retrieval in patients with mild cognitive impairment

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The diagnosis of mild cognitive impairment (MCI) is widely considered a precursor to Alzheimer's disease. Patients with MCI demonstrate significant learning and memory deficits that are often accompanied by reduced prefrontal and medial temporal lobe activation during functional magnetic resonance imaging (fMRI) tasks. Given the known interactions between the prefrontal cortex and medial temporal memory system, cognitive rehabilitation methods that re-engage the prefrontal cortex may ultimately maximize residual hippocampal functioning and improve learning and memory as a result. However, it is currently unknown whether and the extent to which any such changes affect the encoding and/or retrieval phase. Therefore, we examined the overlap in activation changes (post-training minus pre-training) during the successful encoding and subsequent retrieval of object-location associations in a group of nine MCI patients who underwent mnemonic strategy training as part of a randomized controlled trial (Hampstead et al., 2012. *Neuropsychology, 26*, 385-399). These patients underwent two separate fMRI sessions and practiced using mnemonic strategies during three intervening training sessions. In addition to significantly improved memory for the stimuli learned during training, there were robust increases in activation during both encoding and retrieval. Areas of overlap were generally constrained to those commonly associated with the so-called default mode network (i.e., lateral temporal, inferior parietal, and midline areas), which is consistent with the role these regions play in episodic memory recall. Increased activation in the lateral and anterior aspects of the prefrontal cortex and associated subcortical circuits were typically only observed during encoding; a finding that suggests these regions play a unique role in the encoding process. Similar results emerged as participants encoded and retrieved novel associations. Importantly, many of these effects were specific to those receiving mnemonic strategy training since they were not evident in a matched exposure control group of nine additional MCI patients. These results demonstrate that cognitive rehabilitation (re)engages the prefrontal cortex and associated subcortical structures in relatively distinct ways during encoding and retrieval.

Poster #30

Neurochemical predictors of motor recovery in stroke

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Background: Stroke is the leading cause of disability in the United States. This disability could be reduced by restorative therapies. The ability to predict response to restorative therapies would improve patient selection, which would optimize treatment efficacy. Despite vast research on this subject, it is unclear which predictor, or group of predictors, has greatest predictive value. Since motor recovery appears to be influenced by residual function, we proposed here that the extent of cellular injury in spared primary motor cortices (M1) provides valuable prognostic information of recovery. Specifically, we hypothesized that patients with less dysfunctional M1s would have a better chance of recovery, having reserve to boost either cortical activity or behavioral output in response to arm use. We also hypothesized that M1 measures provide insights into biological mechanisms underlying recovery when metrics of stroke severity do not, and combined with these metrics predict recovery better than M1 measures alone.

Methods: Chronic survivors (n=10, 8 males, age 58.7±6.8 years, 32.9±37.7 months post-onset) of an ischemic subcortical stroke leading to arm motor impairment (Fugl-Meyer test, FM_{PRE}, 35.6±18.6) underwent proton magnetic resonance spectroscopic (^{1}H-MRS) and structural MRI evaluations prior to a motor training (PRE). Motor training consisted in repetition of a reach-to-grasp task with the impaired arm for a 12-day acquisition phase spaced over four weeks (90 repetitions/day, 3 days/week). Neurochemicals related to neurons, glia, and the neuronal-glial neurotransmitter system were measured in the hand representation in M1s. Lesion volume (LV) was quantified. FM was also administrated after intervention (POST) and motor recovery was defined as change in FM scores over training (DFM).

Results: *PRE*: There were no correlations between FM_{PRE} or LV and M1 measures.

POST: We observed training-related improvements in FM score with DFM=3.9±2.4. We found evidence that individual or composite measure of ipsilesional neurochemicals predicts the extent of the training-related improvements and their predictive value was stronger than that of FM_{PRE} or LV. By contrast, we failed to detect significant correlations between DFM and FM_{PRE} or LV. The correlations between M1 measures and DFM were greatly strengthened by adding FM_{PRE} and/or LV, especially for the contralesional M1. These combinations also predicted DFM more accurately than did FM_{PRE}, LV or ^{1}H-MRS alone.

Conclusions: We have shown that even in a moderate size sample the M1 neurochemical profile predicts the potential to recover with an intervention, beyond that provided by conventional indices of stroke severity, and combined with these indices improved prediction value. Such a prognostic tool of motor recovery may help clinicians to prescribe restorative therapies with maximal efficacy, by matching treatment with patients who have a sufficient biological target. Since automated ^{1}H-MRS is increasingly available on clinical scanners, a ^{1}H-MRS-based biomarker is feasible in routine practice.

Poster #31

Effects of feedback to enhance self-efficacy on paretic hand use in chronic stroke.

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Background. After stroke, "learned non-use" is sometimes observed in which patients' confidence lags behind physical recovery. Low self-efficacy for use of the affected side can hinder use, which may further limit motor recovery. The purpose of this pilot study was to examine the potential for enhanced self-efficacy to alter paretic hand use after stroke. We used social-comparative feedback, known to influence self-efficacy and motor performance in healthy individuals, to manipulate performance feedback provided to participants with stroke. We hypothesized that participants would increase their paretic hand use following feedback that indicated relative performance success.

Methods. Four participants with chronic stroke performed a reaching task before, after, and at least one day following the feedback manipulation. Participants were instructed to freely choose from either hand to reach presented targets. With feedback, they were informed that their paretic hand reaching performance was better than that of other recruited participants with stroke. Outcome measures were paretic hand self-efficacy for reaching (ASE, range 0-100) and the probability of paretic hand selection (PHS, range 0-1). Further analysis included patterns of target locations selected with the paretic hand. Twelve healthy non-disabled participants who performed the same task without feedback manipulation comprised a control group.

Results. Self-efficacy increased for each of the four participants (average change score for ASE, 11.55) after manipulation. Two participants, who had moderate stroke (Fugl-Meyer scores, 22 and 41), showed an enhanced tendency to use their paretic hand (PHS: from 0.36 to 0.56) with the increased ASE, consistent with our hypothesis. For the other two participants with mild stroke (Fugl-Meyer scores, 61 and 64), the PHSs remained at the same level (0.50-0.53) from baseline. This pattern may reflect a ceiling effect associated with the natural preference of hand use seen in hand selection choices of the control group (PHS for the non-dominant hand, 0.42-0.53). Analysis regarding target locations indicated a possible confidence threshold for paretic hand use. For one of the participants, although the ASE was enhanced after manipulation, the PHS increased only for ipsilateral targets for which there was a high post-feedback ASE (87.50). However, the PHS remained at zero with a relatively low post-feedback ASE (61.25) for contralateral and midline targets.

Conclusion. This pilot work suggests that self-efficacy can be enhanced in individuals with stroke, but the increase may only sometimes be sufficient to affect participants' paretic hand use. A confidence threshold may be required to change hand use probabilities. Future research with a larger sample size is needed to investigate these promising possibilities further. Translation of this experimental work into clinical and applied interventions would also require alternative methods to enhance self-efficacy than the form used here.

Poster #32

Home-based robot-assisted ankle rehabilitation for chronic stroke survivors

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Stroke is the leading cause of disability in the US. Foot drop, a major sequella associated with stroke, contributes to locomotor impairments. Robot assisted repetitive task practice is one approach that has been shown to improve lower extremity function and locomotion in stroke survivors. Robotic training, however, is typically confined to large clinics or research laboratories that few patients have access to. The purpose of the current study was to investigate the effects of home-based robot-assisted ankle rehabilitation on strength, locomotion, and quality of life in chronic stroke survivors.

Four subjects participated in this single group repeated measures design study. Isometric dorsiflexion strength, locomotor function, balance, and quality of life were assessed three times during a 2-week baseline period, three times during a 12-week intervention period, and once after a 4-week follow up period. The intervention consisted of three 60-minute home-base robot-assisted training sessions (Foot Mentor™, Kinetic Muscles Inc.) per week for 12 weeks. Use and performance data from the robotic device was monitored remotely and feedback was given weekly via telephone. All four participants adhered to the intervention protocol with no reports of adverse events. All four particpants demonstrated increases in strength, gait speed, gait distance, and quality of life over time. At week 12; Maximal isometric dorsiflexion force increased by an average of 37 percent, gait speed increased by an average of .2 meters per second, distance on the 6 minute walk test increased by an average of 34.6 meters, and the physical function composite score of the stroke impact scale increased by an average 7.5 points. Limited carryover was observed 4 weeks after the cessation of treatment. No consistent improvements in balance, as measured by the limits of stability test on the Balance Master® (Neurocom) were observed.

These results suggest that home-based robot-assisted ankle rehabilitation improves strength, locomotor function, and quality of life in chronic stroke survivors. Continued treatment, however, may be required maintain the improvements. In addition, balance did not appear to be affected by this intervention. In the changing landscape of health care it is important to investigate alternative methods for delivering physical therapy. Home-based robotic interventions are one such methodology falling under the heading of telerehabilitation. The results presented here provide preliminary evidence supporting the use of home-based robotics for the treatment of distal lower extremity dysfunction in chronic stroke survivors.

Poster #33

Central plasticity of segmental cutaneous nociceptive primary afferents is associated with evoked nociceptive hypereflexia after hemisection spinal cord injury in rats

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The cutaneus trunci muscle (CTM) nociceptive intersegmental spinal reflex results from stimulation of segmental dorsal cutaneous nerves (DCNs) and demonstrates complex neurophysiological plasticity after hemisection spinal cord injury (SCI). The central projection patterns of A and C fibers in DCNs were analyzed 6 weeks after a unilateral T10 spinal cord hemisection. Retrograde axonal tracers, cholera toxin subunit B (CTB) for myelinated A fibers or isolectin B4 (IB4) for non-peptidergic, unmyelinated C fibers, were injected into bilateral T7 and T13 DCNs, one tracer on one side and the other on the other side. Immunohistochemistry was performed on serial transverse sections of the spinal cord at T7 and T13 to measure the projection fields of labeled A and C fibers quantitatively as immunoreactive areas. Synaptophysin, a synaptic vesicle protein, is being used to identify the synaptic terminations of the A and C fibers.

Neurophysiological changes of both Ad and C fiber evoked reflex responses have been shown after spinal cord hemisection injury, both above and below the level of injury and on the side of hemisection and on the uninjured side. In this study we investigated the central projection profiles of bilateral A and C fibers of T7 and T13 DCNs 6 weeks after a unilateral T10 hemisection injury and in uninjured animals. Both A and C fiber projection areas increased overall in T7 and T13 after injury compared to normals. However, the greatest mean increase was seen in C fibers at T7 whereas increases of A fibers were the next greatest at T13. Only C fibers at T7 showed a significant difference between the injured and uninjured sides, with injury side being greater. The rostro-caudal distributions of both A and C fiber projections expanded in both rostral and caudal directions after injury. Not only was there greater area of labeled A and C fiber neurites, they covered a greater territory of the dorsal horn after injury.

After hemisection SCI, the altered projection patterns of DCN A and C fibers in the dorsal horn demonstrate central plasticity of the nociceptive inputs of the CTM reflex. These changes are consistent with the neurophysiological plasticity seen in this reflex after injury. Preliminary work with synaptophysin has shown that these afferent projection area changes also represent overall synaptogenesis following injury. These data demonstrate that anatomical changes of sensory fibers in the CTM pain reflex probably contribute to the "nociceptive hyperreflexia" observed neurophysiologically after hemisection injury. This supports the idea that the CTM reflex could be a good animal model in which to study the neuroplasticity associated with neuropathic pain after SCI that can be quantitatively analyzed, at least for the altered spinal processing of nociceptive signals.

Poster #34

Central plasticity of segmental cutaneous nociceptive primary afferents is associated with evoked dysautonomia after cervical spinal cord injury in rats

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The cutaneus trunci muscle (CTM) nociceptive intersegmental spinal reflex results from stimulation of segmental dorsal cutaneous nerves (DCNs). DCN stimulation also generates a depressor blood pressure response via the autonomic nervous system in normal animals but can generate a pressor response after severe cervical spinal cord crush injury (SCI). The central projection patterns of A and C fibers in DCNs were analyzed 2 and 4 weeks after a C7 bilateral crush SCI. Retrograde axonal tracers, cholera toxin subunit B (CTB) for myelinated A fibers or isolectin B4 (IB4) for non-peptidergic, unmyelinated C fibers, were injected into bilateral T7 and T13 DCNs, one tracer on one side and the other on the other side. Immunohistochemistry was performed on serial transverse sections of the spinal cord at T7 and T13 to measure the projection fields of labeled A and C fibers quantitatively as immunoreactive areas. Synaptophysin, a synaptic vesicle protein, is being used to identify the synaptic terminations of the A and C fibers. Responses of the autonomic system to electrical DCN stimulations were assessed by cannulation of the carotid artery to measure blood pressure.

Blood pressure changes to DCN stimulation in cervical injured rats range from mild dysautonomia to frank autonomic dysreflexia and were usually more pathological with rostral DCN stimulation relative to caudal DCN stimulation. In this study we investigated the central projection profiles of bilateral A and C fibers of T7 and T13 DCNs 2 and 4 weeks after injury and in uninjured animals. C fiber projection areas, more so than A fiber projection areas, increased in T7 and T13 after C7 bilateral crush injury compared to normals. The rostro-caudal distributions of both A and C fiber projections expanded in both rostral and caudal directions after injury. Not only was there greater area of labeled A and C fiber neurites, they covered a greater territory of the dorsal horn after injury.

Current measurements are underway to compare the extent of afferent sprouting at T7 vs T13 to see if the rostral/caudal physiological observations are paralleled by anatomical changes.

Poster #35

Motor control changes in incomplete SCI generated by adding tonic transcutaneous spinal cord stimulation to robotic locomotor training: a test of concept study

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Following spinal cord injury (SCI) there is an altered combination of afferent and supraspinal input to the lumbar neural circuitry for stepping. Tonic transcutaneous spinal cord (dorsal root) stimulation (tSCS) at the lumbar level has been shown to augment locomotor output after SCI in a frequency-dependent manner suggesting that increased afferent input may be able to substitute, to a degree, for decreased supraspinal input. This suggests that tSCS can alter spinal cord motor control. In this test of concept study, we investigated both the acute effect of tSCS on voluntary motor control and the effect of adding tSCS to robotic locomotor training. We studied the change in motor control over the course of locomotor training in terms of reflex modulation and muscle activation patterns during stepping and by clinical scales for gait function and spasticity.

A subject with a chronic C5 motor incomplete SCI underwent a brain motor control assessment (BMCA) both with and without tSCS (at 50 Hz) to determine of tSCS could alter motor control during voluntary tasks. The subject then participated in a series of 36 robotic body weight supported treadmill training sessions to improve gait function and over-ground measures (Timed up and go, Berg balance, 6 minute walk and 10 meter walk over a GAITRite) were serially recorded. The subject then underwent an additional 36 robotic and 24 over-ground gait training sessions combined with sub-motor threshold tSCS (450 microsec biphasic pulses, 50-70 mA, 30Hz) and the same over-ground gait assessments were followed. After training, the patient again underwent a BMCA. H- and posterior root motor (PRM) reflex modulation and muscle patterns dunfing gait, lower extremity motor scores (LEMS), and the Spinal Cord Assessment Tool for Spastic Reflexes (SCATS) were evaluated to further characterize changes in motor control.

With tSCS, the subject demonstrated better muscle activation patterns and speed of muscle activations during voluntary tasks. The subject showed improvements in gait function with locomotor training that were then augmented following locomotor training combined with tSCS. Following the addition of tSCS, reflex modulation became more normal, with H reflexes being larger in stance and smaller in swing. Further analysis of motor control measures are ongoing. This test of concept study shows that traditional rehabilitation strategies to improve locomotion and voluntary motor control CAN be augmented by tSCS and justifies a larger study of combined tSCS and locomotor training.

Poster #36

Real-time optimization of sensory stimulation to improve walking metrics after spinal cord injury

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In normal individuals, spinal neurons integrate sensory feedback from the legs with descending commands from the brain to produce walking. After severe spinal cord injury (SCI), spinal neurons are mostly disconnected from the brain, leading to the loss of voluntary movement below the injury, including the ability to walk. Howere, spinal neurons associated wtih walking - collectively called the locomotor central pattern generator (CPG) - remain connected to the peripheral sensory nervous system from the legs.

Sensory stimulation can recruit the CPG even after SCI, at least to some degree. Our research explores how well the best sensory stimulation patterns can recruit the CPG to assist with walking in humans after severe SCI. Towards that end, we have developed a real-time, closed-loop optimization approach to explore the stimulation space.

Subjects were placed in a robotic gait orthosis, the Lokomat (Hocoma Inc.), to record force output and lower extremity electromyography (EMG) during standardized stepping. Multiple sensory stimulation sites were tested, including: the fibular nerve (both common and superficial), the tibial nerve (both proximal and distal), sartorius muscle afferents, and the posterior roots using transcutaneous spinal cord stimulation (tSCS). These sites were tested both individually and in combination. At each site, a stimulation pattern varying in both frequency and pulse amplitude across the gait cycle was optimized in real time to generate the most normal EMG activity pattern and the best muscle force profile (the least robotic assistance).

So far, the optimization algorithm has shown a posterior root stimulation frequency dependent effect on the EMG pattern during walking, and the algorithm was able to identify the stimulation pattern that generated the best EMG activity and force profile. Ongoing work is exploring the results from the other sensory stimulation sites with other activation patterns. In summary, optimization techniques may be a powerful tool for studies where outcomes can be measured quantitatively and input can be changed on rapid time scales.

Poster #37

Study Protocol: Rationale and methods for a pilot study of brain imaging to predict response to robotic rehabilitation during inpatient rehabilitation

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Robotic therapy has shown benefit for post-stroke rehabilitation of arm hemiparesis. However, most research on robotic rehabilitation has been applied to patients irrespective of the anatomical and functional characterization of their brain lesions. Given the evidence from basic human motor sciences of a dynamic interplay between different brain regions for the control of movement, we hypothesize that lesion characterization by multimodal brain imaging could lead to better prediction of who will benefit most from robotic rehabilitation. This knowledge would inform health policy guidelines for the use of robotic therapy post-stroke. To this end, we are enrolling patients within 8 weeks of first hemiparetic stroke who are admitted for inpatient rehabilitation. In addition to standard multidisciplinary therapy, patients undergo 5 days of additional robot-assisted therapy with the InMotion2 shoulder-elbow planar robot. Prior to robot-assisted therapy, patients are evaluated via MRI imaging for resting state-connectivity and q-space diffusion weighted imaging. Arm impairment is measured via the Fugl-Meyer Assessment and health-related-quality-of-life via the Neuro-QOL computer adaptive test. Preliminary data will be presented.

Poster #38

Improved motor performance in chronic spinal cord injury following upper-limb robotic training

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Background: Recovering upper-limb motor function has important implications for improving independence of patients with tetraplegia after traumatic spinal cord injury (SCI).

Objective: To evaluate the feasibility, safety and effectiveness of robotic-assisted training of upper limb in a chronic SCI population.

Methods: A total of 10 chronic tetraplegic SCI patients (C4 to C6 level of injury, American Spinal Injury Association Impairment Scale, A to D) participated in a 6-week wrist-robot training protocol (1 hour/day 3 times/week). The following outcome measures were recorded at baseline and after the robotic training: a) motor performance, assessed by robot-measured kinematics, b) corticospinal excitability measured by transcranial magnetic stimulation (TMS), and c) changes in clinical scales: motor strength (Upper extremity motor score), pain level (Visual Analog Scale) and spasticity (Modified Ashworth scale).

Results: No adverse effects were observed during or after the robotic training. Statistically significant changes were found in motor performance kinematics: aim (pre 1.17 ± 0.11, post 1.03 ± 0.08, $p=0.03$) and smoothness of movement (pre 0.26 ± 0.03, post 0.31 ± 0.02, $p=0.03$). These changes were not accompanied by changes in upper-extremity muscle strength or corticospinal excitability. No changes in pain or spasticity were found.

Conclusions: Robotic-assisted training of the upper limb over six weeks is a feasible and safe intervention that can enhance movement kinematics without negatively affecting pain or spasticity in chronic SCI. In addition, robot-assisted devices are an excellent tool to quantify motor performance (kinematics) and can be used to sensitively measure changes after a given rehabilitative intervention.

Poster # 39

Initiating Word-Finding Trials with Left-Hand Movement during Anomia Treatment Remaps Frontal Language and Executive Mechanisms

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Chronic aphasias suggest limits to left-hemisphere compensation for damaged language substrates. To facilitate reorganization of these substrates, we developed an Intention Treatment (IT) to shift lateral frontal mechanisms rightward during anomia treatment by initiating word-finding trials with complex left-hand movements. We previously showed that IT successfully does so and that treatment effects generalize to untrained items and discourse. Preliminary data indicate that better improvement during treatment is associated with rightward lateral frontal laterality shifts in nonfluent patients but with rightward posterior perisylvian shifts in fluent aphasias. This paper addresses the effects of IT specifically on frontal cortices associated with executive control and language output.

Methods: Fourteen chronic aphasia patients were equally divided between IT and a Control Treatment (CT), identical to IT except that no hand movement was used to initiate word-finding trials or during response correction. After establishing baseline, patients received 30 treatment sessions over 15 days. There were 3 treatment phases, each of 10 sessions duration. During phases 1 and 2, picture naming was trained. During phase 3, category-member generation was trained. At baseline, post-treatment, and 3-month follow-up, patients participated in event-related, overt category-member generation during fMRI using T2* images. T1-weighted images were collected for anatomic underlay. Operator-assisted ITK-SNAP procedures defined lesion masks, and masked anatomic images were registered into MNI-152 space using non-linear transformation from FSL. AFNI's deconvolution algorithm generated hemodynamic responses (HDRs), subjected to a threshold of $r > 0.345$ ($p<5x10^{-21}$). Then, deconvolved HDR time courses were filtered to reduce speech artifacts, such that voxel-wise correlation of the HDR with at least one of five gamma variates was > .80. Images for each subject were binarized (active vs. not active) and converted to MNI-152 space. Group images showed how many subjects within each group in each voxel showed no activity at either baseline or post-treatment, showed activity at both baseline and post-treatment, showed activity only at baseline, and showed activity only at post-treatment. Only voxels showing changes for more than half of the subjects were interpreted.

Results: Here, we focus only on Broca's region, its right-hemisphere homologue, and dorsolateral prefrontal cortex (DLPFC) bilaterally. For IT, patients lost activity from baseline to pre-treatment in Broca's region, but gained activity in its right-hemisphere homologue. Patients also gained activity in DLPFC from baseline to post-treatment, left more than right. These changes were not seen in the CT.

Discussion: IT switched laterality of Broca's region from left to right. IT engaged left-hemisphere DLPFC. Comparison to CT indicates these frontal-system changes are unique to IT. The right-hemisphere analogue of Broca's region can contribute to rehabilitation-driven word-finding recovery. Engagement of left-hemisphere executive control mechanisms may salvage available language code in left perisylvian cortex to leverage this rehabilitation.

Poster #40

Facilitating neuronal recovery after pediatric traumatic brain injury using optogenetics

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The robustness of plasticity mechanisms during brain development is essential for synaptic formation and has a beneficial outcome following sensory deprivation. However, the role of plasticity on the recovery following acute brain injury in children has not been well-defined. Traumatic brain injury (TBI) is the leading cause of death and disability among children, and long-term disability from pediatric TBI can be particularly devastating. We investigated the altered cortical plasticity 2 to 3 weeks after injury in a pediatric rat model of TBI. Significant decreases in the neurophysiological responses across the depth of the non-injured, primary somatosensory cortex (S1) in TBI rats, compared to age-matched controls, were detected with electrophysiological measurements of multi-unit activity (86.4% decrease) local field potential (75.3% decrease), and functional magnetic resonance imaging (77.6 % decrease). Since the corpus callosum is a clinically important white matter tract that was shown to be consistently involved in post-traumatic axonal injury, we investigate its anatomical and functional characteristics after TBI. Indeed, corpus callosum abnormalities in TBI rats were detected with diffusion tensor imaging (9.3% decrease in fractional anisotropy) and histopathological analysis (14% myelination volume decreases). Whole-cell patch clamp recordings further revealed that TBI results in significant decreases in spontaneous firing rate (57% decrease) and the potential to induce long term potentiation in neurons located in layer V of the non-injured S1 by stimulation of the corpus callosum (82% decrease). These results suggest neurons located in layer V of the non-injured hemisphere are particularly vulnerable to cortical injury. Our current goal is to rescue the hypoactivity of layer V neurons associated with post-TBI using channelrhodopsin-2 (ChR2) activation. For this purpose, via lentivirus infection, we genetically engineered rats to express ChR2 in layer V neurons. We facilitate layer V neuronal excitability in the weeks following the injury in order to recover brain functions. Our preliminary results suggest that optogenetics manipulation of layer V neurons is a promising approach for reversing the adverse neuronal mechanisms activated post-TBI.

Poster #41

Implementation of a multi-center, international, randomized clinical trial in sub-acute stroke patients using wireless health technology

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Objective: To describe the deployment of a wireless remote inertial sensing system to monitor and influence the amount of walking practice during inpatient rehabilitation after stroke.

Background: The amount of active therapy provided to patients during inpatient stroke rehabilitation is estimated to be rather modest. Efforts to objectively and continuously quantify gait training after hemiplegic stroke have been hampered by the cost or insensitivity of commercially available devices to record the slow speeds and asymmetric movements typically seen after stroke. Using a system of wearable inertial sensors and machine-learning algorithms, the SIRRACT trial [Stroke Inpatient Rehabilitation Reinforcement of ACTivity, NCT01246882] aimed to increase the time patients spent walking during inpatient rehabilitation by providing personalized feedback.

Methods: Trial participants were recruited from 12 international (Egypt, India, Italy, Japan, New Zealand, Nigeria, South Korea, Spain, Taiwan, Turkey) and 4 American rehabilitation centers. Inclusion criteria included stroke within the past month requiring inpatient rehabilitation, residual hemiparesis, and the ability to walk at least 5 steps on study entry. During the trial all subjects participated in standard rehabilitative therapies while wearing tri-axial accelerometers at both ankles to record purposeful activities including walking. Sensor data were uploaded nightly to a central server at UCLA for processing. The wireless system used Bayesian machine-learning algorithms and individual gait templates to identify bouts of walking from within daily activity recordings. Parameters were calculated for each walking bout (speed, duration) and each day's activity (number of bouts, average walking speed, total time spent walking, total distance, total steps). Half the participants were randomly assigned to receive sensor-derived feedback about walking performance 3 days a week and the other half to feedback about walking speed only.

Results: 151 participants underwent randomization. Patients with a range of disabilities and initial walking speeds, some as low as 0.2m/s, were included. Over 2000 days of therapy were recorded by study completion. Sensors were actively recording data for more than 8 hours a day. The system identified 37,000 discrete walking episodes containing over 2.5 million steps. Therapy-related activities including cycling, leg extensions, and knee extensions were also automatically identified by the system. Results of the effects of higher levels of feedback will be presented.

Conclusions: This trial demonstrates, for the first time, the feasibility of using inexpensive wireless health technology to remotely monitor the activity of disabled persons in the acute rehabilitation setting. Problem solving challenges for expanding activity monitoring into the outpatient and home-care settings will be discussed.

Poster #42

Development of Virtual Games with Functional Electrical Stimulation for Post-Stroke Hemiplegia

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Virtual reality (VR) games were developed to enhance contralaterally-controlled functional electrical stimulation (CCFES) therapy for restoring hand function to hemiparetic stroke survivors. CCFES enables hemiplegics to open their paretic hand by surface stimulating hand extensors. Stimulation is proportional to degree of unimpaired hand opening as detected by a sensor glove. Thus, volitional nonparetic hand opening produces stimulated paretic hand opening. CCFES features important for motor recovery are: motor intent linked with execution, bilateral movement, and functional task practice. Pilot CCFES studies demonstrated efficacy in chronic (> 6 months) and subacute (< 6 months) hemiplegics.

VR games may optimize CCFES. Existing CCFES includes repetitive hand opening practice cued by audio (at-home, 5 days/week, two hours/day). Although this exercise facilitates repetition, it is not goal-oriented and does not require motor much planning or attention. VR games from literature are independently promising, but have not been combined with electrical stimulation.

VR+CCFES games were designed in collaboration with clinicians, followed by iterative refinement by hemiplegics. Subjects were hemiplegics and able-bodied personnel involved in two ongoing CCFES trials. Games were first evaluated by 3 physiatrists, 2 occupational therapists (OTs), and a biomedical engineer to ensure these criteria were satisfied: 1) game was fun and intuitive; 2) difficulty was appropriate; 3) Goals were achieved using targeted (not compensatory) movements; 4) performance feedback helped motivate improvement; 5) graphics were not distracting; 6) CCFES helps performance. Evaluations were repeated until criteria were met - first by clinicians, then hemiplegics. These games were developed using Unity (Unity Technologies, CA) to run on PCs and used bend sensors to track hand motion (Phidgets, Alberta, Canada).

Paddle Tennis - Players control a paddle to bounce a ball past the opponent's paddle. Graded hand opening is targeted, so vertical paddle position is controlled by paretic hand opening angle. Difficulty is adjusted manually or automatically by changing paddle size, ball speed, and opponent speed. Automatic difficulty increases if hit rate is below 50% and decreases if rate is above 70%. Performance is quantified by score, hit rate, and motor repetitions.

Skee Ball - Players launch balls toward rings at speeds proportional to hand opening rate. Rings move, requiring control of hand opening speed. Difficulty is adjusted automatically or manually by changing ring size. Performance is quantified by score, accuracy, and motor repetitions.

Marble Maze - Players rotate mazes to guide balls out into a bucket. Maze rotation is proportional to hand opening angle, targeting posture maintenance. Difficulty is adjusted by bucket size and adding multiple balls within a maze. Performance is quantified by completion time and score.

Future work will be clinical trials. Treatment will include lab sessions (45 minutes VR+CCFES and 45 minutes OT) and home sessions (VR+CCFES for two hours daily).

Poster #43

Influence of elbow angular spasticity zones on one-trial motor learning in chronic stroke

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Motor learning studies in subjects with stroke have mainly focused on the less-impaired arm to separate confounding influences of motor deficits from motor learning capabilities. One previous study assessing motor learning (error correction) in the hemiparetic arm using a one-trial learning paradigm, showed that error correction strategies were related to both cognitive and arm motor impairment. Subjects with mild paresis used correction strategies resulting in successful one-trial learning, while those with moderate to severe paresis used different strategies or were unable to completely correct movement errors. Zones in shoulder-elbow angular space in which muscles have spasticity and abnormal agonist/antagonist activation during voluntary movements have been identified by the measurement of joint angles corresponding to stretch reflex thresholds (SRTs). Incomplete correction strategies observed previously may be related to movements made beyond angular SRTs that elicit spastic resistance of muscles. This mechanism may confound the interpretation of motor learning studies. Our objective was to assess the influence of spasticity zones on motor learning in stroke. Stroke subjects (Fugl-Meyer scores: 32-61/66) made rapid 35-50° horizontal elbow extension movements from an initial 3° to a final 6° target in 16 blocks of 6-10 trials each. In Session 1, movements were made in mid-range and in Session 2, movements were restricted to a joint range that did not surpass the flexor SRT (outside of the spasticity zone). For each block, movements were alternatively not loaded or loaded by a position dependent load (30% MVC). Subjects were instructed to extend the elbow to the final target in a single fast and accurate movement and correct movement errors as soon as possible. Visual feedback of elbow position and movement speed was provided. Angular positions before correction were used to identify error correction strategies. Changes in load condition from load to no load and vice-versa resulted in overshoot and undershoot errors respectively. In Session 1, subjects corrected errors in 1-4 trials. When movements occurred outside of the spasticity zone, the number of trials needed to correct errors fell to 1-3 with the majority needing only 1-2 trials. Presence of spasticity may confound the results of motor learning studies and should be accounted for while interpreting study results.

Poster #44

Altered obstacle avoidance behaviour in individuals with good arm recovery after stroke

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After stroke, individuals with good sensorimotor recovery of their affected arm report decreased use of the arm in activities of daily living. Decreased use of the affected arm may be associated with undetected motor deficits only identifiable when individuals attempt higher-order tasks that require complex planning and adaptation to produce appropriate interjoint and intersegment coordination. One higher-order motor task, the ability to avoid obstacles while reaching, commonly occurs in everyday environments but is not routinely assessed by clinical scales. We hypothesized that well-recovered people after stroke would be less successful in avoiding an obstacle in the reaching path compared to age-equivalent healthy controls. Obstacle avoidance ability during reaching in a virtual environment (VE) was compared between well-recovered stroke subjects and healthy controls. A VE was developed simulating a grocery store aisle and a commercial refrigerator with sliding doors stocked with bottles on 2 shelves. Subjects reached as fast as possible with their affected/dominant arm for a bottle on one shelf (non-obstructed reaching - template). In random trials (RAND, 30% of 60 trials), the door ipsilateral to the reaching arm closed and partially obstructed the bottle at reach initiation. Subjects were instructed to touch and retrieve the bottle without the hand or arm hitting the door. Arm and trunk movements were recorded with 24 active markers by an Optotrak system. Outcome variables were overall success rates, movement performance and movement quality variables for template (T), successful (Succ), and failed (Fail) avoidance, as well as Succ/Fail divergence points of the endpoint trajectory from template profile (DP=% of reach distance). In T trials, stroke subjects used less wrist flexion, wrist abduction and shoulder rotation compared to controls. In RAND, 36% of controls and 12% of stroke subjects were successful >65% of the time ($z=2.248$; $p<0.05$). For both groups, successful door avoidance was characterized by DP occurring closer to the starting position (Control: DPSucc=11.2±7.0%, DPFail=34.1±37.3%, $p<0.05$; Stroke: DPSucc=20.5±16.1%, DPFail=60.4±33.7%, $p<0.05$). However, the margin of error in the stroke group was about half that of the controls. In addition, stroke subjects had to significantly increase endpoint trajectory length compared to controls to successfully avoid the door. Stroke subjects had residual movement deficits that were revealed through a challenging motor task. The potential of using challenging UL tasks to identify higher order motor control deficits should be considered when assessing post-stroke motor recovery.

Poster #45

Does accelerometer-based feedback increase walking activity during in-patient rehabilitation post-stroke? Preliminary results from a randomized controlled trial.

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BACKGROUND: Regaining independent ambulation is important to those with stroke. During in-patient rehabilitation, patients are generally inactive. Increased walking practice during 'down time' in rehabilitation could improve walking function and outcomes for individuals with stroke. The purpose of this study is to investigate the effect of accelerometer-based feedback on walking activity during in-patient stroke rehabilitation.

METHODS: Participants with stroke wore accelerometers bilaterally around the ankles every weekday during in-patient rehabilitation. Participants were randomly assigned to receive daily feedback about walking activity (feedback group; n=19) or to receive no feedback (control group; n=17). Feedback was provided to participants' primary treating physiotherapists who incorporated the feedback into their usual goal-setting process. Repeated measures ANOVA with group-by-time interaction was used to compare between-group change in walking behaviour from baseline (first two days of monitoring) to the end of the intervention. The following variables were compared: total walking time, total number of steps, average cadence, and duration of the longest bout.

RESULTS: There was no significant increase in total walking time (feedback: 1.1% increase, control: 3.2% increase; p=0.84), total number of steps (feedback: 6.3% increase, control: 3.9% increase; p=0.76), or duration of the longest walking bout (feedback: 13.4% increase, control: 11.0% increase; p=0.82) for the feedback group compared to the control group. However, individuals who received feedback significantly increased their walking cadence compared to those who did not (feedback: 4.6% increase, control: 0.5% increase; p=0.043).

CONCLUSION: Preliminary results indicate that daily feedback of walking activity did not increase the amount of walking completed by individuals with stroke. However, there was a significant increase in cadence, indicating that intensity of walking was greater for those who received feedback than those who did not. Analysis of the full sample (target n=56) will provide further insight into the utility of accelerometer-based feedback in in-patient stroke rehabilitation.

Poster #46

Intensity-dependent effects of tDCS on corticospinal excitability in chronic SCI

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Objective: To investigate the effects of 1 versus 2mA anodal transcranial direct current stimulation (tDCS) on cortical and spinal excitability, and voluntary muscle contraction in patients with chronic spinal cord injury (SCI).

Methods: In this pilot randomized controlled single-blind study, nine chronic SCI patients with some degree of motor dysfunction in the wrist extensor muscle were randomly assigned to one of the three interventions: 1mA, 2mA or sham tDCS, in a crossover design. Each patient received one session of 20 minutes of active anodal tDCS (at 1 or 2mA intensity) or sham on three separate occasions (spaced ≥ 3 days apart), over the right motor cortex forearm area (anode over C3 and return over AF8 based using 3 cm^2 Ag/AgCl Pi-electrodes from Neuroelectrics). Motor cortical excitability was measured with transcranial magnetic stimulation (TMS). Motor evoked potential (MEP) responses from the extensor carpi radialis (ECR) muscle were recorded at rest and during a maximum voluntary contraction. Spinal excitability was measured by F-wave persistence following radial nerve stimulation. Sensory threshold was also obtained. Changes in muscle strength were measured as root mean square (RMS) using surface electromyography during maximal ECR muscle contraction. Outcome measures were recorded at three time points: at baseline (Pre), post-intervention (Post-1) and 20 minutes after the end of the intervention (Post-2). Safety was also assessed following each visit by an adverse event report questionnaire.

Results: There was a significant (p=0.002) increase in MEP amplitude following 2 mA intervention at ~130% baseline (Pre: 0.36 ± 0.1 to Post-1: 0.47 ± 0.11 mV; p=0.002). No changes were seen in active MEP amplitudes, RMS or facilitation. No changes were seen for the other two interventions, active 1 mA or sham. Sensory threshold was significantly reduced following both active anodal stimulation interventions, 1 mA (p=0.002) and 2 mA (p=0.039). Despite the lack of significant changes, active 2 mA intervention showed a tendency for increased spinal excitability (F-wave persistence Pre: 32 ± 12%; Post-1: 41 ± 10%; Post-2: 46 ± 12%). No adverse effects were reported after any of the interventions.

Conclusions: 2mA anodal tDCS intervention is necessary to elevate corticospinal excitability in patients with a long-term spinal lesion affecting the corticospinal tract but some residual muscle function. 1mA anodal tDCS was ineffective to raised corticospinal excitability in this patient group. A combination of this type of non-invasive brain stimulation technique may have promising results when paired with rehabilitation training to improve motor recovery, as has been shown in other neurological diseases.

Poster #47

Neurophysiological signatures of proximal and distal recovery after stroke

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It is generally believed that the recovery of upper extremity paresis in stroke patients is proximal-to-distal: arm segments regain strength before the forearm and hand (Twitchell, 1951; Colebatch et al., 1989). This observation suggests that distal arm strength has greater reorganizational demands, perhaps due to lower redundancy, before it can manifest. If this clinical assumption is true, then we would predict that the corticospinal integrity of a proximal muscle (biceps, BIC) would be preserved or emerge before that of a distal muscle (first dorsal interosseus, FDI). Here we sought to identify the time courses of recovery of corticospinal integrity in proximal and distal cortical representations.

In 14 1st-time ischemic stroke patients, we probed FDI and BIC corticospinal integrity at 1, 4, 12, 24, and 52 weeks after stroke. Corticospinal integrity in the lesioned and nonlesioned hemispheres was assessed with single-pulse TMS at (1) 130% resting motor threshold ("r130") and (2) 100% maximal stimulator output while patients produced approximately 20% maximum voluntary contraction ("aCST").

Our primary outcome was time until emergence of an identifiable motor evoked potential (MEP, >40 μV) in FDI and BIC, arising from the lesioned and non-lesioned hemisphere. We performed a time-to-event analysis with $\alpha = 0.05$. We categorized patients according to whether they had a simultaneous or non-simultaneous FDI-BIC event. We examined if there was a simultaneous or non-simultaneous emergence of FDI-BIC MEPs for each test, comparing across hemispheres. We found no significant difference between hemispheres in time of FDI and BIC MEP onset, for both r130 and aCST.

These preliminary data suggest that in many cases, there may be no neurophysiologic recovery gradient, i.e., that the hand's cortical integrity returns simultaneously with the biceps'. We may find that a gradient of strength and/or control recovery exists behaviorally despite this simultaneity in MEP emergence, which would suggest that other neurophysiologic processes may be responsible for recovery, or that plasticity that we cannot directly measure (for example in the rubrospinal tract) may mediate proximal recovery. Alternatively, it is possible that the chosen time intervals are too coarse to detect subtle longitudinal differences in MEP emergence between proximal and distal cortical representations.

Poster #48

Instrumented Gait Analysis to Differentiate Patients with Mild Cognitive Impairment

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Purpose: The primary purpose of this project is to determine if minimal cognitive impairment in older adults can be predicted using instrumented analysis of psychometric properties of gait.

Rationale: Gait disorders in the community dwelling adult become more prevalent with advancing age. Like gait disorders, the prevalence of dementia also increases with age. Gait abnormalities have been associated with non-Alzheimer's dementias, along with loss of the sense of smell. In addition, persons with early dementia or minimal cognitive impairment (MCI) have demonstrated gait dysfunction that is similar in presentation to that of early Parkinson's Disease. Individuals with early PD demonstrate changes in arms swing, trunk rotation and turning velocity that are detected when using instrumented measurement tools (body worn motion sensors) and not detected using clinical balance tests.

Objective: The main aims of the present study are to 1) show if subjects with MCI demonstrate impaired components of gait using instrumented measurement tools; 2) identify which components can best differentiate between older adults with MCI and those without.

Methods: 29 subjects (10 males, 19 females; age 63.67 years ± 16.18) were recruited as a population of convenience from within a neurology practice, based upon the presence or absence of minimal cognitive impairment determined using the CANS-MCI test for Minimal Cognitive Impairment. Subjects underwent screening for loss of smell using the Quick Smell Test™ protocol. All subjects completed the instrumented Timed up and Go test protocol (iTUG), a test for examination of gait and mobility. This system has wearable wireless inertial measurement units (IMUs) that allow for precise movement recording during functional balance testing activities.

Results: Simple frequency analysis revealed 16 subjects with normal cognition, 13 impaired; smell was normal in 13 subjects, with 16 impaired or absent. Analysis using 1-Way ANOVA identified gait differences between those with minimal cognitive impairment and those without in the TUG parameters of Turn Time, Turn Steps, and Stride Length (%) and smell. Receiver Operator Characteristic Curve (ROC) Analysis of the significant TUG parameters revealed that only the number of Turn Steps possessed discriminate power, with an Area Under the Curve (AUC) of 0.726; smell was determined to have no power with an AUC of 0.320. A test cut off value of ≥ 5.5 steps on the TUG turn was determined to have the strongest validity indices for the determination of possible minimal cognitive impairment (Sn 0.69, 1-Sp 0.38, +LR 1.11, -LR 0.82)

Discussion: Within the limited sample size, results suggest that instrumented analysis of gait parameters, specifically number of turn steps during a Timed up and Go test, may prove an important factor in the identification of those with developing minimal cognitive impairment. Further data collection may strengthen these findings and developing trends.

Poster #49

Turning Stability in people with Parkinson's disease

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BACKGROUND AND AIMS

The ability to turn while walking is essential for daily living activities. Turning difficulties are a common symptom in Parkinson's disease (PD) which is also associated with freezing of gait. In comparison with healthy subjects, turning is usually slower in PD and takes more steps; timing and coordination of the different body segments can also be altered. It is unknown whether the slow turning while walking in people with PD contributes to, or compensates for, their postural instability. The aim of this study was to identify deficits in turning dynamics and stability in subjects with PD.

METHODS

We examined 16 PD subjects (65±6 years, UPDRS III 24.5±7.5, 5 females) and 9 control (CTRL) subjects (68±8 years, 3 females) wearing a set of 16 Motion Analysis reflective markers. Subjects were instructed to walk on a path composed of a mixed route with short straight paths interspersed within 10 turns of 45, 60, 90, 120 and 180 degrees. Each subject performed 12 repetitions: 4 at preferred, 4 at faster, and 4 at slower speed. Body center of mass (CoM), base of foot support (BoS), step length (SL), speed (length of pelvis trajectory divided by time) and cadence during turning were extracted from marker trajectories. In order to limit the effect of the speed in the subsequent comparisons, trials were divided into three groups (Slow, Medium, Fast) depending on the measured mean gait velocity. Kruskal-Wallis test was used to identify significant differences between groups.

RESULTS

The mean angular velocity of the pelvis while turning was significantly slower in PD compared to CTRL. The mean distance between the ankles was significantly smaller while turning in PD compared to CTRL. PD spend a higher percentage of the turn duration with their CoM outside their base of support at medium and fast speed, the percentage increases with speed but 1.5-1.7 times more in PD at medium and fast speed respectively. In PD, the percentage of the turn duration with the CoM outside the BoS was positively correlated with gait speed before and during the turn.

CONCLUSIONS

PD subjects decreased their gait speed more than CTRL before turning and the angular velocity of the pelvis rotation during turns was always slower. PD subjects showed more postural instability during turning related to narrow stance with the body CoM outside of the BoS during turns longer than CTRL, particularly at faster gait speeds. These findings suggest that PD subjects' slower turning speed may be to compensate for their postural instability, which increases as gait/turning speed increases. Rehabilitation interventions that focus on teaching how to widen base of support are needed to help stability in people with PD.

Poster #50

Alterations in upper limb muscle synergies with level of motor impairment in chronic stroke survivors

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Previous studies have shown that motor coordination may be accomplished by assembling task-dependent combinations of a few muscle synergies, defined here as a fixed pattern of activation across a set of muscles. Our recent study of chronic stroke survivors with severe motor impairment showed that some muscle synergies underlying isometric force generation at the hand are altered in the affected arm. To test the hypothesis that alterations in synergy structure vary with the level of motor impairment, we examined spatial patterns of elbow and shoulder muscle activation recorded during an isometric force target matching protocol performed by 24 chronic stroke survivors, evenly distributed across mildly, moderately, and severely impaired groups (Fugl-Meyer score>50, between 26 and 50, and <26 out of 66, respectively). Six neurologically intact, age-matched individuals served as the control group. We applied non-negative matrix factorization to identify the underlying muscle synergies and compared their structure across groups. For all groups, spatial patterns of muscle activation could be explained by task-dependent combinations of only a few (typically 4) muscle synergies. Broadly speaking, the four synergies in the control group, as well as the mildly and moderately impaired stroke groups, were composed of elbow flexors, elbow extensors, shoulder abductors/extensors and shoulder adductors/flexors, respectively. In contrast, the composition of muscle synergies exhibited consistent alterations in the group of severely impaired stroke survivors. Specifically, anterior deltoid was coactivated with medial & posterior deltoids within the shoulder abductor/extensor synergy ("deltoid synergy"). Additionally, the shoulder adductor/flexor synergy was dominated by activation of pectoralis major, with limited anterior deltoid activation. Overall, our results suggest that alterations in the muscle synergies underlying isometric force generation are confined mainly to stroke survivors with severe motor impairment.

Poster #51

Feasibility of relating continuous monitoring of turning mobility to fall risk and cognitive function

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Background

Difficulty turning, or changing direction of walking, is a major contributor to mobility disability, falls and reduced quality of life in older people and people with movement disorders. A complex coupling of balance and locomotor systems, required for turning, gradually deteriorates with age, especially for people with chronic neurological disorders. We speculate that turning speed may be even more sensitive than gait speed to predict future falls, measure benefits or side-effects of treatment and indicate physical health. The *objectives* of this study were to determine the feasibility of continuous monitoring of turning during spontaneous, daily activity and its association with fall risk and cognitive function.

Methods

To date, 7 elderly participants wore 3 Opal sensors on the belt and on each foot throughout 7 consecutive days in their homes. The first day, we validated automatic algorithms of turning identification and duration from the Opals with a mini-camera on the belt pointing at the feet for 30 min, and we conducted a clinical balance assessment test (Mini-BESTest max 28, a score <14 is associated with increased risk for falling). Turning metrics derived from the sensors included average and coefficient of variation (CV) of: 1) number of turns per hour, 2) turn angle amplitude, 3) turn duration, 4) turn rotational rate, 5) number of steps. Neuropsychiatric assessment included cognitive domain z-scores: Executive function, Working memory, Attention/Processing speed, Memory, and Visuospatial function.

Results

The CV of number of turns per hour and the CV of turning amplitude were lower in subjects with lower MiniBESTest scores and these turning variabilities were positively correlated with the MiniBESTest ($r=0.9$, $p=0.006$; $r=0.7$, $p=0.05$). In addition, peak turning speed tended to be smaller in subjects with low MiniBESTest scores. The working memory z-scores were positively correlated with the mean number of steps during turning ($r=-0.76$, $p=0.04$); the memory z-score was associated with turning rotational rate, duration and the CV of number of steps.

Discussion

We show that continuous monitoring of natural turning during daily activities inside or outside the home is feasible for older people who have MCI and/or high fall risk. This preliminary study suggests a less variable, cautious turning strategy in elderly subjects at risk for falls. Mild cognitive deficits was also related to abnormal turning characteristics, consistent with shared neural resources for cognitive and dynamic balance functions. We believe that characterizing functional turning during daily activities will address a critical barrier to clinical practice and clinical trials: objective measures of mobility in real life environment.

Poster #52

Learning strategies of young preterm and term infants

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Purpose: Infants born preterm are at increased risk for developing spastic cerebral palsy, which is characterized by walking limitations due to a reduced ability to move the joints of the legs in an out-of-phase pattern; e.g., flexing the hip while extending the knee. Previous research demonstrates that full-term infants exhibit more out-of-phase hip-knee joint coordination when leg actions are reinforced with activation of an infant mobile, however it is unknown whether preterm infants will exhibit more out-of-phase joint coordination. The purpose of this study is to determine the ability of full-term and preterm infants to (1) learn through discovery the contingency between leg action and mobile activation, (2) demonstrate a greater amount of out-of-phase hip-knee joint coordination when leg actions are reinforced with mobile activation, and to 3) identify strategies defined by the variance and torques used by infants to perform the task.

Method: Fourteen full-term infants and six preterm infants participated at 3-4 months corrected age. On two consecutive days, infants were placed supine under an infant mobile. Day 1 consisted of a 2-min baseline condition (spontaneous kicking) followed by a 6-min acquisition condition (the mobile rotated and played music when the infant moved either foot vertically across a virtual threshold that was individually determined from baseline data). Day 2 consisted of a 2-min baseline condition (no reinforcement), 6-min acquisition condition, and 2-min extinction condition (no reinforcement).

Results: Five full-term and three preterm infants learned the contingency between leg action and mobile activation based on individualized learning criteria. Infants who learned the contingency, but not infants who did not learn the contingency, demonstrated a greater amount of out-of-phase hip-knee joint coordination during the Day 2 acquisition condition as compared to the Day 1 baseline condition. A torque analysis of the kicks of the infants who learned the contingency revealed that the hip and knee muscle contribution to net torque impulse did not change significantly during the baseline and acquisition conditions, however, both significantly increased during the Day 2 extinction condition. Infants who learned the contingency differed in the movement strategy used to increase the amount of mobile reinforcement. Infants (n=2) who crossed a “high” threshold to receive reinforcement (14-20 cm above the table), performed the task by maintaining their feet close to threshold, thereby decreasing movement variance in the vertical dimension. Infants who crossed a “low” threshold (5-8 cm above the table), performed the task by moving their feet progressively higher above the table, thereby increasing movement variance in the vertical dimension.

Conclusion: These results provide the initial scientific support for the development of very early therapeutic interventions using exploratory actions to reinforce more typical hip-knee joint coordination patterns of preterm infants at increased risk for cerebral palsy.

Poster #53

Measuring Cortical Physiology in Stroke Patients with Severe Arm Impairment

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Background: Transcranial magnetic stimulation (TMS) is a key tool for advancing our understanding of stroke recovery mechanisms. Thus far it has been used primarily to examine distal arm muscle representations in patients with relatively mild motor impairment. One reason is that more severely impaired patients often lack active movement of distal muscles and it is often impossible to elicit motor evoked potentials (MEPs) in these muscles. Though more severely impaired patients often retain active movement of more proximal arm muscles, these muscles are more difficult to access with TMS even in healthy individuals, as they have smaller cortical representations and higher thresholds for eliciting MEPs. Here we report a method for using TMS-induced silent periods, rather than MEPs, to measure intracortical and interhemispheric inhibition of proximal muscle representations in patients with severe arm impairment.

Methods: We tested 16 patients with severe arm impairment (Upper Extremity Fugl-Meyer Score=27.0±8.6). During sustained isometric activation of paretic arm biceps or triceps brachii, TMS was applied at 3 different intensities to either the lesioned or non-lesioned hemisphere to measure intracortical and interhemispheric inhibition, respectively. Intracortical inhibition was measured via the cortical silent period (CSP) and interhemispheric inhibition via the ipsilateral silent period (ISP). Measurements were taken 2 times, on separate days. We tested the reliability of these measurements, and their relationships to Fugl-Meyer score and reaching response time.

Results: CSP measurements of intracortical inhibition exhibited moderate to high reliability across all conditions with ICC3,2 values of .57 to .79 ($p<0.02$) for biceps CSP, .68 to .84 ($p<0.005$) for triceps CSP. ISP measurements of interhemispheric inhibition demonstrated moderate to high reliability, with ICC3,2 values of .60 to .81 ($p<0.05$) for biceps in all except the lowest TMS intensity applied, and .53 ($p=0.03$) for triceps ISP at the highest intensity applied. Pearson product-moment correlation analyses demonstrated that Fugl-Meyer Score was positively associated with biceps CSP and negatively associated with biceps ISP. Triceps ISP was also negatively associated with Fugl-Meyer Score. Reaching response time was associated positively with triceps ISP and negatively with biceps CSP.

Discussion: These methods provide a reliable means of measuring motor cortex physiology in proximal arm muscles of severely impaired stroke patients. Our findings suggest that patients with stronger intracortical inhibition of biceps had higher Fugl-Meyer Scores and shorter reaching response times. In addition, patients with stronger interhemispheric inhibition of biceps and triceps had lower Fugl-Meyer Scores, and those with stronger interhemispheric inhibition of triceps exhibited longer reaching response times. These neurophysiologic data are consistent with the pattern of motor deficits exhibited by this population. This study establishes reliable TMS assessment methods for investigation of motor impairment and recovery mechanisms in severely impaired stroke patients, an under-studied population for whom effective treatments are lacking.

Poster #54

TIME COURSE AND MAGNITUDE OF MOTOR LEARNING DURING GAIT REHABILITATION - A PRELIMINARY STUDY

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Introduction: Although motor learning plays a fundamental role in gait rehabilitation, there is limited information about motor learning processes underlying clinical gait training. In addition to evaluating the *efficacy* of gait training, investigation of *time courses* underlying improvements in walking function achieved with clinical gait training is critical for the development of more effective gait training strategies. The purpose of this case study was to evaluate within- and across-session changes in post-stroke gait performance during a 6-week post-stroke gait retraining program.

Methods: An individual with post-stroke left hemiparesis participated in the study (47 year old male, 15.5 months post-stroke, lower extremity Fugl-meyer score = 15). The subject participated in 6-weeks of gait training (3 sessions per week, 36 minutes of training per session) comprising a combination of fast treadmill walking and functional electrical stimulation to plantar- and dorsi-flexor muscles of the paretic ankle. The biomechanical impairments targeted by the intervention (paretic propulsion and swing phase knee flexion) were used as outcome measures of gait performance. During the 1st and 6th weeks, three-dimensional gait analysis was used to measure gait biomechanics during a pre-test (before training session), post-test (after training session), and retention test (48 hours following the training session). Paired t-tests were performed on the stride-by-stride gait data to compare gait performance after versus before 6 weeks of training. Using data from the training sessions during the 1st and 6th training week, online gains in gait performance were computed using the difference between post-test and pre-test. Offline losses were calculated as the difference between retention test and post-test. Retention (motor learning) was computed as the difference between retention test and pre-test.

Results: After 6-weeks of training, the subject showed an increase in over ground gait speed (change=0.19 m/s) and significant ($p<0.05$) improvement in paretic propulsion (62% increase) and swing phase knee flexion (23% increase). Examination of change scores revealed greater online gains, smaller offline losses, and greater motor learning during the 1st versus 6th week of gait training for both paretic propulsion and swing phase knee flexion.

Discussion: This case study suggests that a single gait training session can induce improvements in post-stroke gait performance. Our finding that the magnitude of online gains, offline losses, and motor learning may differ during the early (1st training week) versus late (6th training week) phases of gait rehabilitation is novel and merits further investigation in a larger subject sample. We demonstrate the feasibility and advantage of using within- and across-session changes for systematically tracking motor learning during clinical gait rehabilitation. An in-depth understanding of motor learning processes during gait training can guide the development of novel strategies and dosing regimens to increase the efficacy of each training session and week of gait rehabilitation.

Poster #55

From BCI to AAC and back: towards practical augmentative and alternative communication systems using brain-computer interfaces

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Augmentative and alternative communication (AAC) systems aim to restore communication for individuals with speech or language impairments using residual motion and adapted input devices. For individuals with severe motor impairments who lack the ability to use standard AAC access methods, brain-computer interfaces (BCIs) may offer an alternative by restoring effective communication using control signals extracted directly from the brain. Translating BCIs into useful, practical, and reliable AAC systems will require innovations in multiple areas. In addition to developing and testing investigational methods for intracortical control of external devices (e.g., Hochberg et al, Nature, 2006; Nature 2012), we have also focused on creating customized user interfaces. The *BrainGate Radial Keyboard* is a novel typing interface composed of a radial key layout and a custom ambiguous text entry system. In a recent evaluation by one participant as part of the BrainGate Neural Interface System pilot clinical trials (IDE), the Radial Keyboard yielded higher accuracy and faster typing rates than a standard QWERTY keyboard. The participant, who had tetraplegia and anarthria (inability to speak) due to brainstem stroke, preferred to use the Radial Keyboard, indicating that it was "easier to use". In order to assess the potential utility of BCIs for practical communication purposes, direct comparisons between BCIs and currently available AAC systems are needed. In addition to our ongoing work in creating reliable neural decoders for future use in AAC, we have also recognized an opportunity to leverage affordable off-the-shelf hardware to create improved non-BCI AAC devices, and our academic labs have spun-off a nonprofit organization called the SpeakYourMind Foundation to create and support such personalized AAC solutions.

Poster #56

How does the brain support the recovery of hand function for grasping following surgical hand replantation or transplantation?

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Traumatic amputation of a hand can be reversed through advanced surgical replantation (own hand) or transplantation (other's hand) procedures. Remarkably, with time and practice, these patients can recover function of the re/transplanted hand for grasping and manual interaction with objects. To date, all previous studies of hand re/transplant patients have investigated whether reestablishment of afferent/efferent traffic between hand and brain leads to the reversal of amputation-related reorganizational changes in primary sensory and motor cortex. The goal of the current work is to better understand how the brain supports the functional recovery of manual grasping in these patients. We hypothesize that the recovery of grasp relies on the recruitment of anterior intraparietal cortex, a region known to be critically involved in the sensorimotor transformations necessary for grasp. As patients regain function of their re/transplanted hand for grasping, brain activity associated with grasping with their re/transplanted hand is predicted to closely match activity observed for grasping in healthy controls. To test these predictions, we used fMRI to characterize brain activity associated with grasping using a transplanted hand in patient DR, a 38-year old, right-hand dominant male who suffered traumatic amputation of his left hand in 1998 and underwent allogeneic hand transplantation 13 years later; and patient WH, a 60-year old, right-hand dominant male who had his own left hand surgically reattached hours after traumatic amputation in 2008. During object grasping with their re/transplanted hand (versus a control task involving object touching with the knuckles of the hand, without grasping), both patients showed robust activity within right (contralateral) sensorimotor cortex, spanning the central and postcentral gyri/sulci. The location of this activity was inconsistent with our a priori hypothesis, positioned anterior to the location of anterior intraparietal cortex known to be important for grasping. For both patients, grasp activity partially overlapped with activity defined for the re/transplanted hand using separate sensory and motor paradigms. Likewise, independent region-of-interest analyses showed that motor- and sensory-defined areas for the left hand were more strongly activated for grasping with the left re/transplanted hand versus the control task. To compare with these results, we are currently collecting data from healthy age-, gender-, and handedness-matched control participants using the same grasping, sensory and motor paradigms. Our goal is to not only characterize grasp activity in healthy control participants at the group-level, but to also understand the range of individual-subject variation, for comparison with individual patient results. Notably, both patients tested here also showed evidence of sensory dysfunction for their re/transplanted hand, and, to compensate, relied heavily on visual feedback during grasping. It is possible that the current results reflect atypical grasp activity, indicative of incomplete functional recovery of the re/transplanted hand for grasping.

Poster #57

Wearable audio-biofeedback system for gait rehabilitation of subjects with Parkinson's disease

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INTRODUCTION

Gait difficulties are among the more disabling symptoms of Parkinson's disease (PD) with a strong impact on everyday activities and QoL. Recent studies have shown that rhythmic auditory cues can improve gait performance in PD, still even extensive home-based training programs provide positive but small and not-generalized results (Nieuwboer-et-al, 2007). We hypothesize that similar results can be ascribed to the open-loop modality of supplying the cue. We expect that an approach based on accurate and real-time gait analysis linked with a closed-loop feedback for knowledge-of-performance, may overcome the current limitations and increase treatment efficacy.

METHODS

Assuming that motor learning is a result of intensive but correct repetitions of a motor task, our aim was to design a wearable and stand-alone system able to provide those instructions usually reported to patients by clinicians during gait rehabilitation. Gait parameters object of the treatment are: gait speed, step duration, trunk posture and gait asymmetry. The system was designed to compute these parameters in real-time by means of inertial measurement units (IMUs) and to feedback user's performance through voice messages.

RESULTS

The system is made up of a wearable sensor network with 3 IMUs, two worn on the shoes and one on the lower-trunk, and a smartphone with a user-friendly interface. A new online automatic algorithm was developed to estimate gait events (Ferrari-et-al, 2013). The system then computes gait parameters and compares them with patient's reference values in order to decide whether or not to generate the Audio-Feedback (AF). Reference values are set during a calibration in which the patient is asked to walk at his best performance under the supervision of a clinician. During a training session the AF provides vocal support or tutoring messages based on a chosen number of steps (e.g. every 5 steps). The system also monitors any abnormal inclination of the trunk. The software runs as a stand-alone smartphone app for Android. Noteworthy, it is able to automatically increase the difficulty of the task to follow patient's performance, and to adjust the verbosity of messages to patient's preferences. The system was intensively tested on control subjects and is now in a piloting stage on PD patients.

DISCUSSION

Using a set of custom wearable IMUs with advanced on-board processing capabilities, an application able to perform real-time gait analysis and provide AF to patients with PD was developed. The closed-loop AF system can be comfortably worn with no range restrictions, it can be run by the patient independently, and it realizes a subject-specific rehabilitation program. In the typical scenario of use, the patient walks freely outdoors, e.g. in a park, over single or multiple periods of 30 minutes, receiving AF and in the same time being quantitatively monitored on gait performance.

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Poster #58

Correlation Between Gait Parameters and Balance in Very Young Children. Correlation Between Gait Parameters and Balance inVery Young Children.

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BACKGROUND AND OBJECTIVE: During the implementation of a rehabilitation regimen it is crucial to use validated measurements in order to evaluate treatment effectiveness. This is normally achieved by repeated evaluation by trained personnel that are only sporadically available in rural areas of the country. Evaluation of gait in children is additionally complicated by changes occurring with motor development. A standardized and economic measure of gait would provide important feedback to clinicians regarding the effect of rehabilitation interventions and guide accurate treatment modifications.

The purposes of this study were: i) to identify gait parameters that particularly correlate with motor abilities in young children; ii) to establish standardized normative gait data for future analysis of children with pathological gait.

METHODS: 89 subjects between the ages of 2 and 4 years walked along the GAITRite, a walkway system with pressure sensors that record spatiotemporal parameters. They were also given a modified version of the BERG scale to determine balance. Correlations between gait parameters and balance scores were determined by Pearson and distance correlation to assess both linear and non-linear dependencies

RESULTS: Moderate-to high correlations were found between balance scores and gait parameters (cadence, $r=-0.48$, $p<0.01$; normalized velocity, $r=-0.34$, $p<0.01$; single support, $r=-0.40$, $p<0.01$). Three sub-scores of the balance test were found to have test the largest effect on gait and overall balance: stand with feet together, stand on one foot, and stand with one foot in front.

CONCLUSION: Selected gait parameter could provide a simplified mean to monitor balance and gait development in small children.

Poster #59

Changes in resting-state functional connectivity following BCI-EEG based intervention in sub-acute and chronic stroke patients

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Purpose: We used BCI-EEG driven functional electrical stimulation(FES) of the affected arm, and tongue stimulation(TS) to facilitate upper extremity movement following ischemic stroke. We examined changes in resting state functional connectivity MRI (rs-fcMRI) in the sensorimotor network using 10 minutes eyes-closed resting fMRI. Additionally, we investigated brain-behavior correlation between rs-fcMRI and self-reported measures of hand strength as assessed by the Stroke Impact Scale(SIS).

Materials & Methods: Seven patients(mean age = 64 yrs, 4 males, 6 left hemisphere strokes, between 3 months to 23 months from stroke onset) with persistent mild to severe upper extremity impairment following ischemic stroke received intervention(2 hrs/session, maximum of 15 sessions over 5-6 weeks) using BCI-EEG driven TS and FES. rs-fcMRI images were acquired on a GE 3T MRI scanner as subjects lay in the scanner with eyes closed at 3 time-points- pre(M1), mid(M2), and immediately post intervention(M3). Rs-fcMRI involving connections among 22 regions in the sensorimotor network were examined. The SIS was administered before each scanning session.

Results: Four out of 7 subjects showed significant increase in connection strength from M1 to M2 and from M1 to M3(individual analysis corrected for multiple comparisons, fdr method, $p < .01$). Five of 7 subjects showed increase in number of connections among regions in the sensorimotor network from M1 to M3. Change in connection strength from M1 to M2 moderately correlated with change in hand strength domain of the SIS($r^2 = 0.42$, $r = .65$).

Conclusion: BCI-EEG driven intervention targeted at the sensorimotor network leads to increase in functional connectivity strength as well as the number of connections. These data suggest that BCI-EEG driven FES and TS intervention may promote brain plasticity in sub-acute and chronic stroke patients with variable clinical characteristics.

Clinical Relevance: Analysis of resting state functional connectivity in the sensorimotor network following post-stroke therapy using a brain-computer-interface (BCI)-EEG driven intervention may identify functional connections most amenable to therapy and may help to develop intervention plans to suit specific patient types.

Poster #60

Peripheral nerve injury induces long-term synaptic depression in rat somatosensory cortex

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Evidence suggests that peripheral nerve injury alters the function of the sensory-motor cortices and that these changes may account for sensory dysfunctions often occurring after the injury. We previously demonstrated that peripheral nerve injury results in immediate (Han et al., *Neurorehabilitation and Neuroal Repair* 2013) and long-term (Pelled et al, *Neuroimage* 2007; Pelled et al., *PNAS* 2011; Li et al., *PNAS* 2011) changes in the function of the primary somatosensory cortex (S1) contralateral to the injured limb. Specifically, we found that the injury is accompanied by increases in the activity of inhibitory interneurons, a phenomenon which appeared to be mediated via the transcallosal pathway. However, the cellular mechanisms leading to this plasticity remain unknown. The goal of this research was to investigate the mechanism by which the transcallosal fibers affect neuronal activity after injury. Since one of the main inputs into cortical layer V is transcallosal fibers, whole-cell patch clamp recordings from identified pyramidal (excitatory) neurons in layer V in S1 were collected with and without stimulation of the transacallosal projections. In control and limb denervated rats, we have studies long-term potentiation (LTP) which is one of the major cellular mechanisms that underlie learning and memory. The amplitude of the excitatory post synaptic currents (EPSC) was measured for 30 m following high frequency (100 Hz) stimulation of the transcallosal fibers. The results demonstrated that stimulation of the transcallosal fibers induced 36.93 ± 1.76 % amplitude increase in layer V neurons in control rats (n=11 neurons), but a -16.97 ± 1.0 % amplitude decrease in denervated rats (n=9). Thus, the results suggest that injury decreased the probability of inducing LTP, and increased the probability for long-term synaptic depression. The increases in inhibitory interneurons activity that we have identified previously, might account for the increase in synaptic depression in S1. Increases in synaptic depression associated with peripheral nerve injury might be manifested in the post-injury sensory dysfunction patients often suffer from.