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O1: Assessing Cognitive Function Following Medial Prefrontal Stroke in the Rat

Jessica Livingston-Thomas[1,2], Matthew Jeffers[1,2], Carine Nguemeni[1,2], Molly Shoichet[3], Cindi Morshead[3], Dale Corbett[1,2]

[1]University of Ottawa, Ottawa, ON, Canada, [2]Canadian Partnership for Stroke Recovery, Ottawa, ON, Canada, [3]University of Toronto, Toronto, ON, Canada

Cognitive impairments are prevalent following clinical stroke. However, to date, preclinical research has focused almost exclusively on motor deficits. In order to conduct systematic evaluations into the nature of post-stroke cognitive dysfunction and recovery, it is crucial to develop focal stroke models that affect cognition while leaving motor function intact. Furthermore, in order to investigate potential cognitive post-stroke treatments, it is important that deficits are persistent in the chronic phase. This experiment was performed to evaluate a focal medial prefrontal cortex (mPFC) stroke model using a battery of tests that examined a range of cognitive functions 1-4 months following stroke. Male Sprague-Dawley rats weighing 250-300 g underwent focal ischemia induced in the mPFC using bilateral intracerebral injections of endothelin-1, or sham surgery. Beginning at 1 month post-stroke, cognitive function was assessed using open field, temporal object recognition, object-context recognition, object-placement recognition, attentional set-shifting, light-dark box, spontaneous alternation, Barnes maze, and win-shift/win-stay tests. Prefrontal cortex injury resulted in bilateral damage to the prelimbic and cingulate cortices, extending typically between 4.22 to 1.34 mm anterior to bregma. Animals that underwent stroke surgery exhibited significant changes in all object recognition functions compared to Sham animals ($p<0.05$). Stroke animals also exhibited impaired performance on the Barnes maze ($p=0.012$), and took significantly more trials to learn the second rule in the win-shift/win-stay test ($p=0.013$). Further, they exhibited reduced anxiety-like behaviour in the open field ($p=0.049$). Spontaneous alternation behaviour and locomotion in the open field were not affected. The deficits observed are consistent with some of the key characteristics of prefrontal stroke in humans. Our results show that this model produces persistent deficits in multiple prefrontal cognitive functions, and therefore may be useful for identifying and developing potential therapies for improving cognitive dysfunction in the chronic phase following stroke.

O2: Improving Walking with an Implanted Pulse Generator for Hip, Knee and Ankle Control After Stroke: A Case Report

Nathaniel Makowski, Rudi Kobetic, Lisa Lombardo, Kevin Foglyano, Gilles Pinaults, Stephen Selkirk, Ronald Triolo

Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH, USA

Abstract

Background: Post-stroke gait is limited by compromised volitional joint control that results from muscle weakness, excessive tone, and poor synergist control. About one third of all patients are left with gait deficits after physical therapy and may benefit from assistance during gait. Peroneal nerve stimulators and ankle foot orthoses provide benefit for patients affected by dropfoot, but patients with more severe deficits require additional assistance. Therapeutic and neuroprosthetic effects of a fully implanted pulse generator (IPG) for multi-joint control to assist walking after stroke were evaluated in this case study.

Methods: The participant was a 64 year old male who suffered a hemorrhagic stroke 2 years prior to inclusion in the study. His gait was limited by a combination of muscle weakness, limited independent joint movement, and mild hypertonia. He was a household ambulator with contact guard assistance, but used a wheelchair in the community. He was implanted with an 8-channel IPG and intramuscular electrodes targeting the following muscles: tensor fasciae latae, sartorius, gluteus maximus, short head of biceps femoris, quadriceps, and tibialis anterior (two electrodes). After implantation, a stimulation pattern was tuned to assist with hip, knee, and ankle control. A heel switch in the sole of the shoe on the affected side was used as a trigger to initiate swing and stance phase stimulation. He underwent home exercise with electrical stimulation and stimulation assisted gait training in the laboratory.

Outcome measures included the 10m walk to assess gait speed, 6 minute timed walk to evaluate fatigue, and maximum walk to measure endurance. Assessments were repeated under three conditions: 1) volitional walking at baseline, 2) volitional walking after training, and 3) walking with stimulation after training. Comparisons include evaluating the 1) therapeutic effect (baseline volitional vs. volitional after training), 2) neuroprosthetic effect (volitional after training vs. stimulation after training), and 3) total effect (baseline volitional vs. stimulation after training).

Results: After gait training with stimulation, the participant demonstrated both therapeutic and neuroprosthetic benefits. Therapeutic effects increased walking speed from 0.26m/s to 0.31m/s ($p<0.05$) while neuroprosthetic effects increased walking speed from 0.31m/s to 0.59m/s ($p<0.05$) and total effects increased walking speed from 0.26m/s to 0.59m/s ($p<0.05$). The neuroprosthetic and total effects had a clinically relevant effect size on walking speed of greater than 0.2m/s. Maximum walk distance after training increased from 301m without stimulation to 1418m with stimulation.

Discussion: Multi-joint control by means of an IPG provides a clinically relevant neuroprosthetic effect on walking speed and distance. In addition, there was a trend in therapeutic benefits on walking speed and distance. These data provide proof of concept that a multi-joint IPG control can provide clinically relevant improvements in gait after stroke.

O3: Changes in Synaptic Function and Excitability in Single Neurons Following Transcranial Magnetic Stimulation

N A Matheson, J B H Shemmell, P W Brownjohn, J N J Reynolds

University of Otago, Dunedin, New Zealand

Repetitive transcranial magnetic stimulation, (rTMS) can non-invasively alter the activity of neural circuits for a time outlasting the stimulation period. This has been demonstrated in some studies examining changes in peripheral motor-evoked potentials (MEPs) following application of various rTMS protocols. These prolonged changes have been attributed to the induction of synaptic plasticity. At a single neuron level however, the effects of rTMS are not well understood and the induction of synaptic plasticity or prolonged changes in cellular excitability have not been demonstrated.

Using a rat model we investigated the effects of TMS on activity characteristics of single pyramidal neurons. *In vivo* intracellular sharp-electrode electrophysiological recordings were made from single cortical neurons in urethane-anaesthetized Wistar rats, during the application of TMS. Spontaneous neuron activity was recorded in response to single pulse and rTMS. In addition, post-synaptic potentials (PSPs) elicited using electrical or magnetic stimulation of the ipsilateral hemisphere were investigated both pre and post rTMS.

Action potentials and PSPs were reliably obtained following single pulse TMS, delivered at intensities much lower than those used in many clinical settings. During rTMS trains, spontaneous rhythmical neuronal activity was disrupted and in some cases, neuronal firing was induced. Following rTMS, neuronal excitability was altered as indicated by lasting changes in rheobase current and spontaneous activity. Furthermore, both long term potentiation (LTP) and long term depression (LTD) were observed following particular combinations of rTMS protocols.

These results provide the first indication of the effects that both single pulse and repetitive TMS have on cortical neuron excitability and synaptic plasticity. With a better understanding of these effects it is hoped rTMS protocols may be more effectively targeted to specific neural circuits, in order to optimize clinical treatment of neurological disorders.

O4: Enhancing Cortical Representational Plasticity with Non-Invasive Direct Current Stimulation to Accelerate Upper Limb Recovery in Quadriplegia

Kelsey Potter-Baker, Daniel Janini, Nicole Varnerin, David Cunningham, Vishwanath Sankarasubramanian, Ken Sakaie, Frederick Frost, Ela Plow

Cleveland Clinic Foundation, Cleveland, OH, USA

Current published work suggests that a minimum of 9 months of rehabilitation is required to elicit significant improvement in upper limb function following incomplete spinal cord injury (iSCI). With over 12,500 new cases and a prevalence of 337,000 in the U.S. alone, however, such extensive rehabilitation programs are impractical. Here, we tested the hypothesis that the brain and its residual descending pathways represent the most spared, and hence ideal, innovative targets for maximizing and accelerating upper limb recovery in iSCI. In particular, since loss of representation of weaker muscles in the motor cortex exaggerates muscle weakness and limits recovery following iSCI, we aimed to boost inherent adaptive plasticity of weak representations using transcranial direct current stimulation (tDCS). We hypothesized that tDCS would accelerate increases in weak muscle cortical representational plasticity while also enhancing excitability of their descending pathways to paretic limbs to ultimately maximize functional outcomes following rehabilitation. To test our hypothesis, eight patients with chronic iSCI received either upper limb rehabilitation with tDCS (2 mA anodal) to motor cortical representations of weak muscles or rehabilitation alone. Representational plasticity was measured using TMS before and after treatment and diffusion tensor magnetic resonance imaging (DTI) quantified sparing of descending tracts. Functional recovery and muscle strength was assessed before and after treatment. We found that patients who received tDCS plus rehabilitation demonstrated significant focal increases in the cortical representation of their weaker muscle, where its excitability increased by 60% ($p<0.05$). Representational plasticity changes were associated with gains in motor function and muscle strength. In addition, level of recovery was related to cortical tract integrity, wherein patients that demonstrated the most recovery had greatest tract sparing following their iSCI ($r=0.97$; $p<0.0001$). Our results suggest that long-term pairing with tDCS applied to the motor cortex could result in significant functional improvements by facilitating more permanent plasticity of weaker cortical representations. Further, descending tract integrity, as measured with DTI, may serve as a valuable prognostic marker of impairment and functional recovery potential.

O5: Detection and Predictive Value of Fractional Anisotropy Abnormalities in the Acute Stroke Patients

Jasmine Wang, Gottfried Schlaug

Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

Background: A decrease in fractional anisotropy (FA) of the ipsilesional corticospinal tract (CST) distal to stroke lesions in subacute and chronic patients has been associated with poor motor outcomes, but it is unclear whether tract-FA in the acute stroke phase predicts outcome.

Methods: Thirty-eight patients underwent an assessment of their motor impairment acutely and at 3 months using the Upper Extremity Fugl-Meyer (UE-FM). MR images, including diffusion tensor images (DTI) and derived FA values, obtained <3 days after stroke, were overlaid with a probabilistic CST derived from healthy elderly subjects to define two regions of interest (cerebral peduncle (CP) and a slice of the CST consisting of the second subsequent slices caudal to the stroke lesion (nearest slice – NS)).

Results: The FA laterality index (LI) for NS-ROI and CP-ROI were significant, but modest predictors of 3-months outcome ($R2 = 0.114$, $p=0.032$; $R2=0.14$, $p=0.042$). UE-FM ($R2=0.710$, $p<0.001$) was a better predictor than FA values in univariate analysis, though comparable to prediction using the CST lesion load (wCST-LL) ($R2=0.709$, $p<0.001$). In multivariate analyses controlling for initial UE-FM, CST-LL, and Days-of-Therapy, neither the FA LI for the cerebral peduncle ROI (partial correlation $r=0.014$ $p=0.88$) nor the nearest slice ROI (partial correlation $r=0.025$, $p=0.72$) significantly contributed to the overall model prediction of 88% of the variance in the UE-FM at 3 months.

Conclusion: FA changes of the CST can be detected near the ischemic lesion in the acute phase after stroke, but these changes offer only modest predictive value to motor outcomes at 3 months

T1: Use of Inertial Sensors for Determining Kinematic Characteristics of Infant Leg Movement

Ivan A. Trujillo-Priego, Beth A. Smith

University of Southern California, Los Angeles, CA, USA

Our overall goal is to use inertial sensors to determine the quantity, type and quality of infants' leg movements performed across a full-day measurement for further use in the differentiation of infants with typical, delayed or impaired neuromotor development. Here we describe an algorithm to calculate kinematic characteristics of leg movements.

Inertial sensor data were collected from 12 infants with typical development for a period of 8-13 hours per day. There were 2 months between visits and a total of 3 visits per infant. An inertial sensor was attached to each leg, recording simultaneously accelerometer and gyroscope measurements at 20Hz. In previous work, we developed and validated a threshold-based algorithm where each pause or change of direction of the limb is counted as a discrete movement. Here we determined the duration, average acceleration, and peak acceleration of each movement. The duration of each movement was computed by counting the number of samples when the acceleration magnitude was above baseline until it crossed the baseline for a second time. Consequently, acceleration magnitude was obtained for each of these samples and average acceleration and peak acceleration of each movement was calculated.

Infants produced average movement durations that ranged from 0.23 to 0.33 seconds per movement, with average accelerations ranging from 1.59 to 3.88 m/s^2 and average peak accelerations from 3.10 to 8.83 m/s^2.

Our results showed that there is a range of leg movement duration and acceleration values produced by infants across visits. Future work will focus on the analysis of movement features based on the age and developmental level of infants and identification of the differences between infants with typical, delayed or impaired neuromotor development.

T2: Moving Towards Clinical Integration of Accelerometers to Measure Real-World Arm Use After Stroke

Kathryn S Hayward[1,2], Janice J Eng[1,3], Lara A Boyd[1], Bimal Lakhani[1], Julie Bernhardt[2,4], Catherine Lang[5]

[1]University of British Columbia, Vancouver, Canada, [2]University of Melbourne, Melbourne, Australia, [3]Vancouver Coastal Health Research Institute, Vancouver, Canada, [4]Latrobe University, Melbourne, Australia, [5]Washington University, St Louis, USA

Purpose: The ultimate goal of upper limb rehabilitation after stroke is to promote use of the paretic upper limb in everyday activities outside the clinic or laboratory. One way to capture such use is with accelerometers, which have gained growing acceptance as a tool to objectively index upper limb use in real-world environments. This review aims to explore the feasibility of accelerometers to measure upper limb use after stroke and the translation of accelerometers into clinical practice. We will discuss: 1) how accelerometers determine *amount* of use; 2) the *reliability, validity and sensitivity to change* of accelerometry data; 3) how the accelerometer signal can be turned into *clinically meaningful data*; and 4) the practicalities of building an *accelerometry data collection protocol*.

Discussion: Accelerometers determine amount of upper limb use by measuring acceleration and provide an activity count for each instance in time or epoch. Activity counts can be summed to index magnitude of use and epochs of activity can be summed to index duration of use. Accelerometry data have good test-retest reliability and agreement with movement repetitions, standardized measures of upper limb function and brain recovery; but there is conflicting evidence surrounding the sensitivity of accelerometry data to change after upper limb training interventions. Despite growing evidence of their accuracy as a tool to measure upper limb use in real-world environments, a critical challenge to facilitating widespread clinical uptake of accelerometers is the ability to transform the data recorded by the accelerometer into information that has clinical relevance. Most recently, a new method for transforming accelerometry data into clinically-meaningful information has been evaluated. This approach involves second-by-second quantification of the magnitude of use from both limbs; and the relative contribution of each upper limb to the activity count. Outputs from this approach have been used to provide clinically-meaningful information of use in real-world environments for clinicians, patients, family, and caregivers. While this provides the impetus for greater uptake of accelerometers in research and clinical settings, it also increases the need for consistency when building an accelerometry data collection protocol to enable comparison and data pooling. Variables to consider include device selection (uniaxial or multiaxial), epoch length (i.e., <1-sec vs. 1-sec vs. 15-secs), duration of monitoring (i.e., 1-day vs. 3-days vs. 7-days), number of devices to wear and body position (i.e., paretic and non-paretic wrist) and use index metrics (i.e., magnitude, duration).

Conclusion: By growing a consistent pool of data, a deeper understanding of what stroke survivors actually do in their everyday lives will be gained. Such information has the potential to positively impact on the ability of researchers and clinicians to objectively evaluate function, set benchmarks for treatment, as well as develop and adapt rehabilitation protocols on an individual basis.

T3: Effect of task-specific training on Eph/ephrin expression after stroke

Dong-Hee Choi[1,2], Jin-Hee Ahn[1], In-Ae Choi[1], Ji-Hye Kim[1], Jongmin Lee[1,3]

[1]Center for Neuroscience Research, Institute of Biomedical Science and Technology, Konkuk University, Seoul, Republic of Korea, [2]Department of Medical Science, School of Medicine, Konkuk University, Seoul, Republic of Korea, [3]Department of Rehabilitation Medicine, School of Medicine, Konkuk University, Seoul, Republic of Korea

Stroke is the leading cause of adult disability because of the brain's limited capacity for repair. Several processes like angiogenesis, neurogenesis, axonal reorganization and synaptic plasticity act in concert to restore eurological functions after stroke. Although some degree of spontaneous axonal sprouting occurs after stroke, regeneration of lesioned axons and formation of new connection is limited. The Eph/ephrin signaling has recently been identified to play important roles in activity dependent plasticity, angiogenesis and stem cell diffenetiation in adulthood as well as axon guidance in development.

To investigate the effect of task-specific training on Eph/ephrin expression in peri-infarct area and corticospinal tract after stroke, we compared the expression of Eph receptors and ephrin ligands in cortex and corticospinal tract between control and task-specific training group.

Rats were subjected to photothrombotic infarct. Task-specific training (single pellet reaching, 300 pellets/day or 20min/day) was initiated at 5 days post-stroke and continued for 4 weeks. Behavioral tests such as single pellet reaching test, parallel bar test and cylinder test were performed at 1 day pre-stroke, 5 days post-stroke, 1 week, 2, 3, and 4 weeks post- task-specific training. The expressions of Eph receptors (EphA2 and EphA4) and ephrin ligands (ephrinA1, ephrinA2, and ephrinA5) in the peri-infarct cortex, pyramid and spinal cord at 2 and 5 weeks after stroke were determined by Western blot analysis. Eph/ephrin expression levels after stroke were compared them after task-specific training for 1 week or 4 weeks.

Task-specific training group showed significantly better recovery in the behavioral tests. The expression level of ephrinA1, ephrinA2, and ephrinA5 in the pyramid containing corticospinal tract was increased at 2 W post-stroke. Increased ephrin A1 and ephrinA5 levels at 2 W post-stroke were decreased in ipsilateral pyramid by task-specific training for 1 W. However, increased expression levels of ephrinA1, ephrinA2, and ephrinA5 in the pyramid at 5 W post-stroke have not changed by task-specific training for 4 W.

These data suggest that task-specific training alter the expression of ephrin ligands in corticospinal tract at 2 W post-stroke. Controlling expression of ephrin ligands and task-specific training may be a promising therapeutic strategy to enhance stroke recovery.

T4: Brain-Computer Interface Assisted Stroke Rehabilitation with Multimodal Feedback

Christoph Guger[1,3], Rupert Ortner[2], Danut Irimia[2]

[1]g.tec medical engineering GmbH, Schiedberg, Austria, [2]Guger Technologies OG, Graz, Austria, [3]g.tec neurotechnology USA Inc., Albany, USA

A brain-computer interface (BCI) allows to analyze brain activity in order to control an avatar or rehabilitation training device. Important for a successful outcome of the rehabilitation procedure is that the mental activity is paired with the avatar movements or rehabilitation device movements.

The study was performed with two patients who had a stroke 4 years earlier (P1, female, 40 years old) or 2 month earlier (P2, female, 61 years old). P1 suffered a complete paralysis of her left hand, but had normal right hand movements. The hand performance of P2 was measured with a 9 hole PEG test and showed that the right arm needed about twice as much time to complete the test.

Both patients performed the motor imagery (MI) session by imagining left or right hand movements according to an instruction on a computer screen. Then the BCI system analyzed the EEG data and controlled an avatar hand movement on the computer screen and simultaneously controlled a functional electrical stimulator (FES) that stimulated the corresponding hand. Therefore, the patients' could see the virtual hand movement and the real hand was simultaneously also moving.

After 10 training sessions of 30 minutes each with P1 and 21 training sessions with P2 the success of the procedure could already be shown. P2 was able to move the paralyzed hand herself without the BCI and FES and P2 could perform the 9-hole PEG test with similar speed for both hands.

This shows that the training is successful and more patients are undergoing further tests currently.

T5: Awareness Assessment and Communication Tool for Patients with Disorders of Consciousness

Christoph Guger[1,3], Rupert Ornter[2]

[1]g.tec medical engineering GmbH, Schiedlberg, Austria, [2]Guger Technologies OG, Graz, Austria, [3]g.tec neurotechnology USA Inc., Albany, USA

Up to 43% of coma patients are misclassified as vegetative when actually possessing (at least minimal) conscious abilities. EEG based Brain-Computer-Interfaces (BCI) can detect command following in patients with altered states of consciousness. In this study a BCI system was used that combines three different BCI approaches - auditory P300, tactile P300 and motor imagery (MI) - in one portable tool for bedside awareness detection and (if possible) communication with the goal to enhance correct patient classification.

The electroencephalogram (EEG) yields brain wave patterns which can be assigned to a deliberate response to external stimuli or orders. These intentionally influenced states are detected by mindBEAGLE via a Mann-Whitney U test ($p<0.05$) and provide information about the conscious reaction of the patient. In the case of positive results, modulating these brain wave patterns on purpose allows the patient to answer YES/NO questions for communication means. This can be done by using generic classifiers or by training patient-specific classifiers (training time: P300 ~5min, MI ~20min). Prototypes of the BCI system have already been evaluated using healthy subjects and patients with locked-in syndrome. For patients the tactile P300 paradigm yields accuracies of 80.0% (σ 33.5%) in a two-stimulator setup (YES questions) and 55.3% (σ 27.3%) in a three-stimulator setup (YES/NO questions). The MI approach gives an accuracy of 80.7% (σ 14.4%) for healthy subjects (YES/NO questions).

With the combination of three different BCI technologies to assess awareness in coma patients, mindBEAGLE is opening doors for locked-in patients to call attention to their conscious mind state and to re-enable basic communication.

T6: Two-Week Administration of Neuropathic Pain Medications Fails to Prevent the Development of Cutaneously Evoked Autonomic Dysreflexia After High Thoracic Spinal Cord Transection in Rats

Keith Tansey, Jumi Chung, Hyun Joon Lee

Emory University/Atlanta VA, Atlanta, GA, USA

In uninjured, pentobarbital anesthetized Long Evans rats, electrical stimulation of thoracic segmental dorsal cutaneous nerves (DCNs) generates a stimulation frequency and nociceptive afferent subtype specific cardiovascular response. To varying degrees, depressor blood pressure (BP) responses and heart rate (HR) increases are seen. We previously found that cervical (C7) spinal cord crush/incomplete injury gives rise to 3 different pathophysiological BP responses to DCN stimulation at 2 weeks, a normal-like depressor response evoked by all DCNs, a dysautonomia response where mixed depressor and pressor effects are evoked from different DCNs, and a pressor response like autonomic dysreflexia (AD) evoked by all DCNs. In all 3 injury groups, the HR increases evoked by DCN stimulation showed prolonged elevation. We also found that the severity of BP pathology is positively correlated with the extent of DCN C fiber sprouting in the dorsal horn and that the prolonged HR responses are correlated with increases in DCN A fiber sprouting there.

We have now used a complete T2 spinal cord transection model to produce consistent pressor BP and increased HR responses to stimulation across all DCNs. In this model, we have continuously (twice daily for 2 weeks following injury) administered 3 neuropathic pain medications commonly used clinically in spinal cord injury (SCI). We used an opioid (Buprenorphine, 0.05 mg/kg), a non-steroidal anti-inflammatory drug (Meloxicam, 1 mg/kg), and an anti-epileptic medication (Gabapentin, 50 mg/kg) to test the hypothesis that continuously treating "pain" could perhaps limit the development of nociception induced autonomic dysfunction after severe high thoracic SCI. Following injury and treatment, segmental DCN stimulation still generated AD cardiovascular responses with pressor BP and increased HR effects in all 3 drug groups. Buprenorphine generated even greater BP increases with caudal (T12, L1) DCN activation. We are currently evaluating whether A and C fiber sprouting in the dorsal horn of these animals tracks with our physiological findings.

T7: Sildenafil for Stroke Recovery

Christopher Walter, Steven Edgley, Jacob Smith, Mary Paulter, Lorie Richards

University of Utah, Salt Lake City, USA

Introduction: Post-stroke hemiparesis causes long-term disability. Current rehabilitation approaches are limited. Pharmacological agents that may enhance neuroplasticity have the potential for increasing post-stroke motor recovery. Sildenafil citrate, a phosphodiesterase type 5 inhibitor, shows promise for reducing post-stroke motor impairments as it has been shown to promote angiogenesis, axonal growth and reorganization, neurogenesis, and motor function in rodents with stroke. The mechanism of action is proposed to be the increases in cyclic guanosine monophosphate-adenosine monophosphate and vascular endothelial growth factor facilitated by sildenafil, both of which are implicated in neuroplasticity.

Methods: In a pilot, randomized clinical trial, we examined the ability of sildenafil to promote motor recovery from stroke in humans who were within 11 days of stroke. Seven individuals who were admitted to inpatient post-stroke rehabilitation were randomized to either the sildenafil (25 mg) or placebo group based on baseline Fugl-Meyer Assessment scores. Participants took the drug or placebo for 14 days. Each individual completed their usual post-stroke rehabilitation. Their motor skill was tested at baseline, 1 month post-discharge, and 3 months post-discharge. The primary outcome was the Fugl-Meyer Asssment, a measure of post-stroke motor impairment.

Results: Three participants were randomized to the sildenafil group and 4 to the placebo group. Groups were not significantly different in baseline Fugl-Meyer Assessment score [41.25(27.45sd) for sildenafil group; 53.00(25.42sd) for the placebo group; $T(6) = -0.63$, $p > 0.55$]. The 18.5 (13.03sd) point gain in motor ability experienced by the sildenafil group was not significantly different from the 17.25(5.12sd) point gain experienced by the placebo group at 1 month post discharge. However, at the 3 month follow-up testing, the sildenafil group had improved 33.33 (9.24sd) points from baseline on the Fugl-Meyer Assessment while the placebo group only improved 14 (8.04sd) points, $T(6) = 4.55$, $p < 0.005$. There were no drops in blood pressure outside of the expected blood pressure variation experienced after stroke. There were no adverse events while taking the drug. One sildenafil participant did have evidence of new stroke activity at the 1 month follow-up that was deemed due to high levels of cerebral athersclerosis.

Conclusions: The results of this small pilot trial suggest that sildenafil citrate given during acute rehabilitation may promote greater motor recovery from stroke compared to rehabilitation by itself. Further research is needed to confirm this effect and to establish its safety in this population.

T8: Targeted Memory Reactivation to Improve Motor Learning

Brian Johnson1, Steven Scharf2,3, Kelly Westlake1

[1]*University of Maryland School of Medicine, Department of Physical Therapy & Rehabilitation Science, Baltimore, Maryland, USA,* [2]*University of Maryland Sleep Disorders Center, Baltimore, Maryland, USA,* [3]*University of Maryland Medical Center, Division of Pulmonary and Critical Care Medicine, Baltimore, Maryland, USA*

Background: It is evident that memories are 'replayed' throughout the course of sleep to strengthen neural networks involved with each memory and may occur during quiet wake as well.

Purpose: To determine whether motor memory reactivation during quiet wake or sleep, via auditory cues classically conditioned to upper extremity (UE) performance during wake, can improve UE motor function. We hypothesize that replaying the same auditory cues experienced during UE motor training will improve throwing accuracy compared to receiving no cues between sessions.

Methods: The training protocol involves (1) repetitive throwing of a small ball using the non-dominant UE to five unique visuospatial targets, and (2) auditory cues distinctively paired with each target. Spatial metrics of throwing accuracy are collected at 5 time points (baseline, post initial training session, post 8 hour interval, post second training session, and at 1 week retention). We have recruited 17 young, healthy adults and randomized them into the following groups, that are differentiated by the 8 hour between-session time interval: (1) wake with auditory cues, (2) wake without auditory cues, (3) sleep with auditory cues and (4) sleep without auditory cues.

Results: Data has been collected for six subjects evenly distributed between the wake groups. Preliminary results between the first participant in each wake group demonstrate that auditory cues enhanced spatial accuracy compared to no cues. Further data collection and analysis are planned. Results of this research are expected to serve as the first step towards a follow up study to enhance UE training protocols in individuals post-stroke.

T9: Centralized Open-Access Research (COAR): A Database for Stroke Rehabilitation

Keith Lohse[1], Lara Boyd[2], Catherine Lang[3]

[1]*Auburn University, Auburn, Alabama, USA,* [2]*University of British Columbia, Vancouver, British Columbia, Canada,* [3]*Washington University School of Medicine, St. Louis, Missouri, USA*

Background: There is a wealth of quality experimental data from randomized controlled trials (RCTs) to support evidence-based physical medicine and rehabilitation, but most of these data are "unstructured". That is, these results are published in different formats, to varying degrees of completeness, and across many different journals to which researchers may not have access. Thus, the goal of the current project is to systematically extract data related to participant outcomes, participant demographics, and clinical methods, and organize these data into a machine readable format. Having open-access to such a database will allow clinicians and researchers to quickly and easily visualize results and explore the relationships between variables in hundreds of RCTs.

Method: A systematic search of electronic databases yielded 2,892 results. Screening titles and abstracts by our exclusion criteria left a pool of 398 RCTs (although further manuscripts maybe excluded as data extraction/ full text review continues). We are currently piloting data extraction protocols using two independent coders at Auburn University. "Pilot" meta-data from the first $n = 42$ RCTs, constituting $k = 90$ independent groups of participants, are presented. Specific aims were to (1) quantify the dose of therapy in groups who received "conventional" therapy and (2) quantify the magnitude of improvement at terminal and follow-up assessments for these groups. Other exploratory graphical analyses are presented to highlight the flexibility of the database for data visualization.

Results (ad interim): Conventional therapy in these RCTs had a median duration of 28 [14, 42] days, shown as median [IQR], with a median time scheduled for therapy of 20 [14.4, 30] hours. The median age for participants in these groups was 64.7 [62.2, 68.2] years and participants started the RCT 38.4 [21.2, 170.7] days following stroke. At the terminal assessment ($k = 32$), the median Cohen's d was 0.51 [0.25, 0.73] and the median therapy duration was 28 [14, 42] days. At the follow-up assessment ($k = 17$), the median Cohen's d was 0.86 [0.45, 1.07] and the follow-up assessment came 180 [87, 181] days following the baseline assessment.

Conclusions: Systematic reviews will always be important and necessary; a centralized open-access database will allow clinicians and researchers to quickly aggregate and visualize relationships between prognostic variables on an unprecedented scale. Although data extraction continues, the database has already allowed detailed examination of "conventional" therapies as they are delivered in RCTs. Although data support a benefit to these therapies, shown in terminal and follow-up effect-sizes, it is not clear what aspects/conditions of therapy produce these changes. A current challenge facing the database is how best to systematically quantify exclusion criteria used in different RCTs to effectively describe populations under study.

Prospero Registry: CRD42014009010

T10: Exercise, Cognition and Brain Imaging in Parkinsonism - Study Design

Katrijn Smulders[1], Laurie King[1], Martina Mancini[1], Daniel Peterson[1,2], Patricia Carlson-Kuhta[1], John Nutt[1], Brett Fling[1], Fay Horak[1,2]

[1]Oregon Health & Science University, Portland, OR, USA, [2]VA Portland Health Care Systems, Portland, OR, USA

Background: Parkinsonian gait and balance impairments have been associated with cognitive deficits. Hence, it may be helpful to integrate cognitive challenges into mobility training. We present a study design to evaluate a novel, cognitively challenging mobility rehabilitation program in patients with PD and in patients with FGD. Objectives are 1) to determine the effectiveness of a cognitively challenging Agility Boot Camp (C-ABC) exercise program on mobility, cognition, and brain connectivity and 2) to determine whether baseline mobility and cognitive deficits, and the integrity of locomotor brain circuitry predict responsiveness to exercise in patients with Parkinson's disease (PD) and Frontal Gait disorders (FGD).

Methods: Eigthy patients with PD (n=60) or FGD (n=20) will participate in this randomized, crossover design study. The C-ABC intervention will consist of 80 min group exercise sessions, 3 days per week for 6 weeks. Exercises include mobility skills such as fast walking in different directions, boxing, lunging, and navigating an agility course, focused on a variety of postural domains. Cognitive challenge is added by memorizing sequences, dual tasking and inhibiting actions. The education control program will consist of a 90 min education program in a group setting, once a week for 6 weeks, and 5x30 minutes of active relaxation with audiotape at home for 6 weeks. Hence, each program consists of 240 minutes of activities every week. The primary outcome measure is dynamic balance using the MiniBESTest. Secondary outcome measures include of objective mobility measures, cognitive tasks and locomotor functional connectivity. Pre- and post-testing will occur before and after each phase of the cross-over interventions.

Results: The first two groups of subjects have completed the study. Eighteen subjects with PD and two FGD patient were enrolled in the study. Two subjects dropped out because of injury (n=1) and inaccurate diagnosis (1 FGD patient later diagnosed as corticobasal syndrome).

Conclusions: We hypothesize that mobility, cognitive, and functional connectivity of the locomotor circuitry will improve after the C-ABC program but not after the control intervention. We also hypothesize that FGD patients with freezing of gait, executive dysfunction and reduced white matter tracks between the penduncolopontine nucleus (PPN) and frontal cortex will be poor rehabilitation candidates.

T11: Freezing of Gait in Parkinson's Disease: A Stopping Deficit?

Katrijn Smulders[1], Daniel Peterson[1,2], John Nutt[1], Fay Horak[1,2], Brett Fling[1]

[1]Oregon Health & Science University, Portland, OR, USA, [2]Portland VA Medical Center, Portland, OR, USA

Recent studies suggest that patients with Parkinson's disease (PD) with freezing of gait (FOG) are impaired in response inhibition (e.g. Stroop task, GoNoGo task). Moreover, neuroimaging studies show that patients with FOG have loss of white matter in nodes that are part of the "stopping" network, comprising the presupplementary motor area (preSMA), right inferior frontal gyrus (rIFG) and subthalamic nuclei (STN). This network is particularly important for global stopping of motor actions as assessed in stop signal reaction tasks (SSRT). We evaluated the performance of PD patients with and without FOG on the SSRT and related stopping performance to the structural integrity of the neural stopping network.

Methods: 14 patients with FOG (FOG+) and 9 PD patients without (FOG-) completed the SSRT. Probabilistic structural connectivity of the right hemisphere's stopping network was performed to identify quantity and quality of fiber tract connections between 1) preSMA IFG, 2) preSMA STN and 3)IFG STN.

Results: There were no significant differences between FOG+ and FOG- patients on the SSRT (p=.467). Also, microstructural integrity of fibers comprising the stopping network did not differ between FOG+ and FOG- (all p's>.60). Across all participants, we observed a negative association between the SSRT and connectivity quality of the rIFG (r=.452, p=.030) and preSMA (r=0.509, p=.013), but not with STN (.323, p=.133). These significant associations between SSRT and connectivity values were driven by the FOG+ group (r = 0.55, p = 0.04 for both); there were no significant correlations between SSRT and structural integrity of the stopping network in the FOG+ group alone.

Conclusion: Our results do not support a global stopping deficit in PD patients with FOG. Similar to previous work in healthy subjects, in patients with FoG we report a strong association between inhibitory network structural integrity and SSRT performance. This suggests that integrity of the tracts to/from the rIFG and preSMA is related to the ability to stop a prepared motor action in PD patients with FOG.

T12: Upper Extremity Functional Evalulation by Virtual Fugl-Meyer Assessment Using Kinect in Hemiplegic Stroke Patients

Won-Seok Kim[1], Sungmin Cho[2], Hyunwoo Bang[2], Nam-Jong Paik[1]

[1]Department of Rehabiliation Medicine, Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-do, Republic of Korea, [2]School of Mechanical and Aerospace Engineering, Seoul National University, Seoul, Republic of Korea

Introduction: Virtual home-based rehabilitation is an emerging area in stroke rehabilitation and functional assessment tool is essential to monitor recovery and provide current function-based rehabilitation. We developed the virtual Fugl-Meyer Assessment (FMA) tool using Kincet (Microsoft, USA) and validated it for hemiplegic stroke patients.

Methods: Forty-one patients with hemiplegic stroke were enrolled. Thirteen items were selected among 33 items for motor FMA in the upper extremities (UE). One occupational therapist assessed the motor FMA while recording the UE motion with Kinect. Saved data were analyzed and virtual FMA score were calculated by one postgraduate student who was blind to real FMA score. Principal component analysis and artificial neural network learning were used. Prediction accuracy for each 13 item was calculated and correlations between real and virtual FMA scores were analyzed.

Results: Prediction accuracies ranged from 65 to 87% in each item and were above 70% in 9 items. Correlation of summed score for 13 items between real and virtual FMA was high (Pearson's correlation coefficient=0.873, p<0.0001). Correlation between total UE FMA (66 in full score) and virtual FMA (26 in full score) was also high (Pearson's correlation coefficient =0.799, p<0.0001).

Conclusion: Virtual FMA using Kinect is valid to assess the UE function of stroke patients and may be useful in the setting of unsupervised home-based rehabilitation.

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T13: Hebbian-Type Motor Cortex Stimulation Promotes Motor Learning in Chronic Stroke Patients

Julianne Freeman[1], Gregory Kowalski[1], Kate Revill[1], Marc Haut[2], Samir Belagaje[1], Gerald Hobbs[2], Cathrin Buetefisch[1]

[1]Emory University, Atlanta, GA, USA, [2]West Virginia University, Morgantown, WV, USA

After stroke of primary motor cortex (M1) or its corticospinal projections, plasticity in the peri-infarct tissue supports recovery of hand function. Transcranial magnetic stimulation (TMS) of ipsilesional M1 can enhance cortical plasticity and rehabilitative training-related motor learning. Hebbian-type TMS is a type of TMS that is administered concurrently with motor training. During Hebbian-type TMS, training movement-related increases in electromyographic (EMG) activity triggers subthreshold TMS over the M1 contralateral to the training hand in order to apply stimulation when M1 is involved in generating training movements. Because Hebbian-type TMS is more effective in enhancing motor learning than random TMS (Buetefisch et al., 2004; 2015), there is considerable interest to study the effect of Hebbian-type TMS in rehabilitative training of patients after stroke involving M1 or its corticospinal projections. Here we determine whether Hebbian-type TMS enhances motor training-related improvement of paretic hand function in chronic stroke. 16 patients (9M, 64.37±9.21 years) with impaired hand function due to chronic stroke involving M1 or its corticospinal projections participated in a randomized double-blinded placebo-controlled trial. Participants completed 5 days of motor training where they were asked to execute auditory paced wrist extension movements in a way that a cursor, encoding the movement's velocity and angle, hit a target on a computer screen. Increases in movement-related EMG activity of the extensor carpi ulnaris muscle (ECU), a muscle supporting the training movement, were used to trigger TMS or sham stimulation. Therefore, training movements were paired with subthreshold Hebbian-type TMS (n=8) or sham stimulation (n=8) over the ECU hot spot of ipsilesional M1. The effects of the two interventions on movement kinematics (peak acceleration of wrist extension), motor function (Jebsen-Taylor Test) and M1 reorganization were determined before and immediately after and one month after training. To measure M1 reorganization we extracted the asymptote and slope-parameter of a stimulus response curve collected with TMS (range: 35%-80% stimulator output) over the ECU hot spot (Devanne et al., 1997). At baseline the treatment groups were comparable in respect to their main outcome measures. Participants who received Hebbian-type TMS experienced greater training-related changes in kinematics (acceleration=+74.73%), hand function (Jebsen=-19.84%) and cortical excitability (asymptote=+8.51%, slope-parameter=+14.34%) than those who received sham stimulation (acceleration=+32.42%, Jebsen=-8.72%, asymptote=+2.171%, slope-parameter=-14.50%). The improvement in hand kinematics and function persisted in both groups for 4 weeks. The results suggest that Hebbian-type TMS enhances training-related gains in hand function when applied to patients with chronic stroke affecting primary motor output. Greater functional improvements may be associated with a larger shift in M1 organization as indicated by increased excitability of the ECU representation. Prior to final analysis, 4 additional subjects will be recruited by August 2015 to meet our targeted number of 10 participants in each treatment group.

T14: Capturing Recovery Potential After Severe Stroke: How Individuality Drives the Need for a Multimodal Approach

Kathryn S Hayward[1,2], Sue Peters[1], Jason L Neva[1], Katie P Wadden[1], Lara A Boyd[1]

[1]University of British Columbia, Vancouver, Canada, [2]University of Melbourne, Melbourne, Australia

Background: Determining how to reliably identify with upper limb recovery potential after stroke has received growing attention. People with the greatest recovery potential are more easily identified by the ability to physically move their upper limb early after stroke (e.g., shoulder abduction or finger extension). It is much more challenging to identify the recovery potential of stroke survivors who are unable to demonstrate such physical movements early; typically these individuals suffer from more severe disability. To provide a more sensitive evaluation of recovery potential, transcranial magnetic stimulation (TMS) and diffusion-weighted magnetic resonance imaging (DW-MRI) have been identified as possible tools.

Aim: To explore potential indicators of recovery potential derived from TMS and DW-MRI in a group of stroke survivors with severe (Fugl Meyer Upper Limb [FM-UL] score <26/66 points) and chronic (>6 months) upper limb disability.

Methods: Five stroke survivors (mean: 61 years old, 45 months post stroke) completed a clinical assessment of upper limb impairment (FM-UL) and activity (Wolf Motor Function Test [WMFT] rate). Participants underwent a TMS assessment and DW-MRI, from which the presence of seven potential indicators of recovery potential were documented: TMS, paretic upper limb motor evoked potentials (MEPs) elicited from the ipsilesional hemisphere and transcallosal inhibition (TCI) elicited from both ipsilesional and contralesional hemispheres; DW-MRI, ipsilesional corticospinal tract (CST), ipsilesional posterior limb of the internal capsule (PLIC) and ipsilesional tracts extracted to a constrained motor connectome (CMC). Lastly, participants practiced an implicit motor learning task. Exponential curve fitting was used to categorize individual patterns of change across practice as 'learners' (improved performance) or 'non-learners'.

Results: Stroke survivors demonstrated marked upper limb impairment (FM-UL mean 15, range 7-23) and activity limitations (WMFT mean rate 14 repetitions, range 9-20). TMS assessment provided limited information: an ipsilesional MEP was not detected in any participant, and three did not demonstrate ipsilesional or contralesional TCI. From DW-MRI, three out of five participants had extractable ipsilesional CST tracts, five had extractable ipsilesional PLIC tracts and four had extractable ipsilesional tracts using the CMC. Lastly, four participants were identified as 'learners'.

Discussion: This study demonstrates variability in both the brain and behaviour of people with severe upper limb disability after stroke. Only the most severe participant (FM-UL score of 7) demonstrated consistently poor performance across all indicators. Clinical and neuroimaging outcomes provided the most information to characterise an individual's recovery potential. Novel to this study, we evaluated an individuals 'learning' capacity. Despite, the severity of disability and reduced microstructural properties, the majority of participants were identified as 'learners'. Taken together, this suggests that clinical outcomes combined with neuroimaging metrics and a learning evaluation provide a broader basis upon which to assess the recovery potential of individuals with severe upper limb disability.

T15: Refinement of the PREP Algorithm for Predicting Recovery of Upper Limb Function After Stroke

Cathy Stinear[1], Suzanne Ackerley[1], Winston Byblow[1], Alan Barber[1,2], Anna McRae[2], Henrietta Lee[1]

[1]University of Auckland, Auckland, New Zealand, [2]Auckland District Health Board, Auckland, New Zealand

The PREP algorithm was developed to predict the potential for recovery of upper limb function for individual patients within days after stroke. The original dataset included 40 people with first-ever mono-hemispheric ischemic stroke. This study tested the algorithm with a larger, more heterogeneous sample, in order to refine it prior to implementation in clinical practice. We recruited 85 patients with upper limb weakness within 3 days after stroke, and used the PREP algorithm to predict the level of upper limb function at 12 weeks. Assessments were made at baseline and 12 weeks, and upper limb therapy dose was recorded. Sixty-nine patients completed the 12 week assessments, and were categorised as having achieved the predicted level of upper limb function, over-achieved, or under-achieved. This dataset was then compared with the original dataset from 40 patients. There were three main findings that influenced the plan for subsequent clinical implementation of the algorithm. First, transcranial magnetic stimulation (TMS) could elicit motor evoked potentials in the paretic wrist extensor muscles of all patients with a Shoulder Abduction Finger Extension (SAFE) score of 5, 6 or 7. This means that patients with a SAFE score in this range can be given a prognosis for Notable recovery of upper limb function, without TMS assessment. This reduces the proportion of patients requiring TMS assessment from 58% to 40%. Second, a larger proportion of patients in this study under-achieved relative to their predicted level of upper limb function, compared with the original dataset (25% vs. 5%, $P = 0.005$). This effect was driven by patients with a Complete recovery prognosis (35% under-achieved vs. 6%, $P = 0.035$), as there were no differences between the groups for patients in other prognosis categories (all $P > 0.2$). Patient characteristics with a Complete prognosis were similar between the two datasets, except for a substantially lower recorded therapy dose in the present study ($P < 0.001$). A home exercise programme was implemented to increase therapy dose for patients in this category. Thirdly, we found that a higher proportion of patients in this study over-achieved, and exceeded their predicted recovery of upper limb function (17% vs. 8%, $P > 0.05$). While this was not statistically significant, it indicates that some patients can recover better than expected. Therefore when implementing the algorithm the prognosis is used to indicate the minimum level of function that the patient is likely to achieve, leaving open the possibility that they may exceed this level. The PREP algorithm is now being implemented in clinical practice with these modifications, with prognoses being provided to patients and therapy teams. Results of this implementation study are expected in 12 months.

T16: Post Stroke Sensory Loss is Associated Self-reported Functional Status and Changes in Gait Speed Following Intervention Post Stroke Sensory Loss is Associated Self-reported Functional Status and Changes in Gait Speed Following Intervention

Jane E. Sullivan, Roberto Lopez-Rosado

Northwestern University, Chicago, Il, USA

Purpose: While sensation has been reported to be an important predictor of functional outcome following stroke, intervention studies commonly report on subject baseline characteristics and outcomes primarily in motor function and activity domains. It is far less common for sensory status and outcomes to be reported. The purpose of this study was to determine the association of baseline sensory status and outcomes for post stroke participants in an intervention study. Subjects: Participants were 15 community ambulators with unilateral hemiparesis secondary to chronic stroke (8.21 + 4.36 years) who participated in a single group pretest-posttest, follow-up design 6-week study involving sensory amplitude electrical stimulation (SES) delivered via sock electrode during standing activities.

Methods: Baseline sensory scores and change scores on functional outcomes were analyzed using Pearson Product-Movement Correlation Coefficients. Significance $p < 0.05$. Baseline sensory status of the hemiparetic foot was assessed via the Perceptual Threshold of Electrical Stimulation (PTTES) and Monofilament testing. Intervention outcomes were assessed using the 10 Meter Walk Test (10MWT), Activities-Specific Balance Confidence (ABC) test, Berg Balance (BBS), Monofilaments, the Stroke Rehabilitation Assessment of Movement (STREAM), Stroke Impact Scale (SIS) and SIS 16. Effect sizes were calculated for each of the outcome measures.

Results: Mean baseline sensory scores on the PTTES were 22.5 mA (+ 11.2); mean baseline monofilament scores were 134.53g (+ 203.8). Baseline Monofilament scores were not significantly correlated with baseline PTTES scores (r= -.074). Baseline PTTES scores were significantly correlated with scores on the baseline SIS (r= -.679), SIS 16 (r= -.824), and SIS mobility subscale scores (r=. -715). Baseline PTTES scores were significantly correlated with change scores on the SIS 16 (r=.631) and ABC (r= -.777). Baseline Monofilament scores were correlated with baseline scores on the SIS participation subscale (r= -.649). Baseline Monofilament scores were correlated with change scores on the 10MWT (r=.715). There were moderate effect sizes for changes in Monofilament (0.301), STREAM (0.5) and 10MWT (0.57) scores. Conclusions: In this cohort of individuals with chronic stroke, greater sensory impairment was associated with lower self-reported baseline functional status; however larger gains in gait speed. Clinical Relevance: Assessing sensory status of stroke subjects may help determine the impact of sensory dysfunction on outcomes and assist clinicians to individualize interventions based on patient characteristics. Clinical Relevance: Assessing sensory status of stroke subjects may help determine the impact of sensory dysfunction on outcomes and assist clinicians to individualize interventions based on patient characteristics.

T18: Is Infarct Location a Predictor of the Degree of Post-Stroke Motor Recovery?

Sudhir Karthikeyan[1], Matthew Jeffers[1], Anthony Carter[1,2], Dale Corbett[1,2]

[1]University of Ottawa, Ottawa, Canada, [2]Canadian Partnership for Stroke Recovery, Ottawa, Canada

Stroke is a leading cause of neurological disability and a majority of patients have long-term motor impairments, often as a result of damage to the motor cortex and/or striatum. While both humans and animals show spontaneous recovery following stroke, little is known about how injury location affects the recovery process. This information is essential in order to develop new therapies to enhance recovery.

In this study we used endothelin-1 (ET-1), a potent vasoconstrictor, to produce focal infarcts in the forelimb motor cortex, the dorsolateral striatum or both the cortex and striatum in male Sprague-Dawley rats. The spontaneous recovery profile of the animals was followed over an 8-week period using four behavioural tasks assessing motor function and limb preference to identify how recovery varies depending on injury location. Infarct volumes were derived from MRI 72 hours post-stroke.

All three models resulted in functional deficits on the Montoya staircase ($p < 0.002$), beam ($p < 0.017$), and cylinder ($p < 0.001$) tasks but no significant impairments were seen in the adhesive removal task. The three groups demonstrated distinct patterns of recovery on the behavioural tasks with the combined cortical plus striatal group having the largest and most persistent impairments overall. There were no significant differences between groups for total hemispheric infarct volume.

These results suggest that damage to the striatum is an important predictor of the level of post-stroke motor impairment. Moreover, the pattern of recovery is not simply dependent on lesion volume but on lesion location and the behavioural test employed. All three models produce sustained motor impairments that will be valuable in assessing novel, adjunctive post-stroke therapies.

T19: Sensory-Driven Motor Recovery in Poorly Recovered Subacute Stroke Patients

Cheryl Carrico[1], Kenneth C. Chelette[1], Elizabeth Salmon-Powell[1], Laurie Nichols[1], Emily Salyers[1], Lumy Sawaki[1]

[1]University of Kentucky, Lexington, KY, USA, [2]Cardinal Hill Hospital, Lexington, KY, USA

Stroke continues to be a major public health concern in the United States. Therapeutic interventions after stroke can support motor recovery by capitalizing on neuroplastic change (reorganization of the central nervous system). Intensive, task-oriented motor training is an example of an intervention that aligns with principles governing neuroplastic change. While this type of training has been shown to effect neuroplastic change and improve motor function in stroke survivors with *mild to moderate* motor deficit, no proven benefit has emerged in cases of *severe* motor deficit (ie, virtually no wrist and finger movement). On the other hand, several lines of evidence indicate that sensory input can drive neuroplastic change and that manipulating sensory input via peripheral nerve stimulation (PNS) can enhance outcomes of motor training. Here, we report on our pioneering evidence that in cases of *severe* motor deficit after stroke, PNS can enhance outcomes of intensive, task-oriented training. In this double-blind, sham-controlled, randomized study, 71 subjects with subacute stroke (ie, 3-12 months from stroke onset) received 2 hours of PNS immediately prior to 3 hours of intensive, task-oriented training (18 sessions total). PNS condition (active versus sham) was the only independent variable. We evaluated motor performance according to the upper extremity motor score of the Fugl Meyer Assessment (FMA) score at baseline; immediately after completion of the total intervention period; and at 1- and 4-month follow-ups. Results indicated that active PNS can enhance outcomes of motor training significantly more than sham PNS. Also, only the active PNS group had continuous improvement evident at all longitudinal follow-ups. Our forthcoming analysis of data collected via transcranial magnetic stimulation will substantiate potential correlations between neuroplastic change and motor performance change. The overall impact of this study is to help expand effective rehabilitation options for stroke survivors with highest need. Our long-term goals include enhancing the translational potential of this paired intervention (ie, development of portable PNS for clinic and home use; streamlining PNS protocols for time-sensitive environments, such as home exercise or reimbursement-dependent settings).

T21: Does the Attentional Status Affect the Efficacy of the Neurofeedback-Based Rehabilitation?: Preliminary Analysis Using Functinoal-NIRS-Mediated (Neurofeedback) System Neural Repair Mechanisms

Hiroaki Fujimoto[1], Masahito Mihara[2], Noriaki Hattori[1], Megumi Hatakenaka[1], Hajime Yagura[1], Teiji Kawano[1], Hideki Mochizuki[2], Ichiro Miyai[1]

[1]Morinomiya Hospital, Osaka, Japan, [2]Osaka University, Suita, Osaka, Japan

Background: Balance impairment is a major problem for patients with stroke and other neurological diseases, which limits their activities of daily living (ADL). We previously reported that the supplementary motor area (SMA) potentially plays an important role in balance recovery after stroke. Based on the hypothesis that the SMA facilitation would augment balance recovery after stroke, we have confirmed that the SMA facilitation by functional near-infrared spectroscopy mediated neurofeedback (fNIRS-NFB) have positive effect on balance ability in healthy subjects (ASNR annual meeting 2014, Washington DC). Thus we have started the proof-of-concept study to confirm the favorable effect of SMA facilitation by fNIRS-NFB on balance recovery in stroke patients (the results of interim analysis would be presented in 45th SfN annual meeting 2015).

Aim: The aim of this study was to assess whether the attentional status as assessed by Frontal Assessment Battery (FAB) and Digit Span (DS) affects the efficacy of the fNIRS-NFB for balance recovery in stroke patients.

Methods: Ten stroke patients (7 males, Age : 59.8± 9.5, 115.7± 18.6 days from onset) with subcortical lesions, who admitted to Morinomiya hospital (Osaka, JAPAN) for inpatient intensive rehabilitation participated in this study. Clinical assessment including Berg Balance Scale, 10m walking test (10MWT), 3m-Timed Up-and-go test (TUG), and FAB or DS were assessed before (t0), immediate after (t1), and two weeks (t2) after fNIRS-NFB based intervention. In addition to standard rehabilitation therapy up to 180min/day for 7days per week, all patients participated 6 sessions of fNIRS-NFB targeting the SMA activity combined with mental practice using motor imagery of gait and postural related task (3 times /week x 2 weeks). Based on the FAB and DS, patients were divided into high (FAB$\geqq$15) and low attention (FAB<15 or backward DS$\leqq$2) group.

Results: Age and post-stroke duration were comparable for two groups. The value of each clinical assessment at t0 was set as 100%. At immediately after and 2 weeks after the fNIRS-NFB, 10MWT was 68.5% (t1) and 57.5% (t2) in high group, and 77.0% (t1) and 71.7% (t2) in low group. TUG was 72.8% (t1) and 66.3% (t2) in high group, and was 85.6% (t1) and 73.6% (t2) in low group. Although high group showed a trend for better gait improvement than low group, it did not reach the statistical significance.

Conclusion: Although there was several limitations in this study including small number of patients, our finding suggest that attentional status might affect the efficacy of fNIRS-NFB intervention in stroke patients.

T22: Effectiveness of Active Pedaling Combined with Sensory Electrical Stimulation on Gait Performance in Subacute Stroke Patients: A Multicenter, Sham-Controlled Randomized Controlled Trial

Koki Ikuno[1,2], Tomofumi Yamaguchi[3], Ken Fuchigami[2,4], Soichiro Koyama[5], Hiroyuki Kobayashi[6], Masaki Kitaura[7], Saori Kawaguchi[8], Kanako Fujikawa[9], Hikaru Matsunaga[10]

[1]Nishiyamato Rehabilitation Hospital, Kanmaki-cho, Nara, Japan, [2]Kio University, Koryo-cho, Nara, Japan, [3]Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan, [4]Kishiwada Eishinkai Hospital, Kishiwada-shi, Osaka, Japan, [5]Kawamura Hospital, Gifu-shi, Gifu, Japan, [6]Sumiya Rehabilitation Hospital, Wakayama-shi, Wakayama, Japan, [7]Wakayama Physical Therapy College, Wakayama-shi, Wakayama, Japan, [8]Terashita Hospital, Wakayama-shi, Wakayama, Japan, [9]Kyowakai Hospital, Suita-shi, Osaka, Japan, [10]Tokyo Bay Rehabilitation Hospital, Narashino-shi, Chiba, Japan

Background: Pedaling is used for locomotor training because it induces muscle activities very similar to locomotion. Recent studies have shown that sensory electrical stimulation (ES) combined with additional therapy is behaviorally more effective than ES alone in the rehabilitation of patients following stroke. Thus, it has been hypothesized that ES during pedaling can improve gait performance more than ES or pedaling alone in patients with stroke. The aim of the study was to examine the combined effects of pedaling and ES on gait performance in subacute stroke patients.

Methods: This study was a multicenter, randomized, assessor masked, sham-controlled clinical trial. Participants were randomly allocated to one of the following three groups: pedaling plus ES (P-ES), pedaling plus sham ES (P-sham ES), and ES alone. P-ES and P-sham ES groups performed 15 min of pedaling at their comfortable speed. ES was applied to the affected leg via surface electrodes over the quadriceps and tibialis anterior muscle without muscle activation throughout the pedaling. In ES alone, ES was applied for 15 min while sitting on the chair. All groups received each treatment 5 days per week for 3 weeks in addition to the conventional inpatient rehabilitation. Outcome measures included 10-meter walking test (10mWT) and 6-minute walking test (6MWT) recorded at baseline, after 3 weeks of the treatment, and at 6-week follow-up.

Results: Of the 69 participants, 23, 24, and 22 individuals were assigned to the P-ES, P-sham ES, and ES alone, respectively. Two patients dropped-out during interventions. Ten patients discontinued the study before the follow-up assessments. Following an intention-to-treat approach, data from 57 participants were analyzed. No significant differences were found between groups at baseline. A mixed-model analysis showed a significant interaction of the group and times ($p < 0.05$). All treatments resulted in significant improvements in 10mWT (P-ES: from 0.52±0.27 m/s to 0.70±0.29 m/s, P-Sham ES: from 0.38±0.23 m/s to 0.46±0.27 m/s, ES: from 0.58±0.26 m/s to 0.69±0.34 m/s) and 6MWT (P-ES: from 168.2±115.7 m to 237.2±107.5 m, P-Sham ES: from 138.6±91.5 m to 159.5±107.6 m, ES: from 171.0±80.1 m to 223.5±140.2 m) after 3 weeks of the treatment compared to baseline ($p < 0.05$). Post hoc analysis showed that the P-ES and ES groups showed significantly better improvement in comparison with the P-sham ES group at the end of the 3-week treatment and in the 6-week follow-up ($p < 0.05$).

Conclusion: Pedaling combined with ES and ES alone in addition to inpatient rehabilitation can induce greater improvement in gait performance than pedaling alone in subacute stroke patients.

T23: Prevalence of Growth Hormone Deficiency in Chronic Traumatic Brain Injury

Lisa Kreber, Grace Griesbach, Mark Ashley

Centre for Neuro Skills, Bakersfield, CA, USA

This study examined the prevalence of growth hormone deficiency (GHD) in patients with traumatic brain injury (TBI) during the post-acute phase of recovery and whether GHD was associated with increased disability, decreased independence and depression. A secondary objective was to determine the accuracy of insulin-like growth factor-1 (IGF-1) levels in predicting GHD in patients with TBI. Anterior pituitary function was assessed in 235 adult patients with TBI through evaluation of fasting morning hormone levels. Growth hormone levels were assessed through provocative testing, specifically the glucagon stimulation test. GHD was diagnosed in a significant number of patients, with 45% falling into the severe GHD (<3 ug/L) category. IGF-1 levels were not predictive of GHD. Patients with GHD were more disabled and less independent compared to those patients who were not GHD. Those patients with more severe GHD also showed decreased levels of cortisol and testosterone. Symptoms of depression were also more prevalent in this group. In addition, patients with severe GHD had delayed admission to post-acute rehabilitation. This study confirms the high prevalence of GHD in patients with TBI and the necessity to monitor clinical symptoms and perform provocative testing to definitively diagnose GHD.

T24: Study Design: Identifying Carpal Tunnel Syndrome in Stroke Recovery using Ultrasound

Chen Lin, Aaron Loochtan, Lisa Hobson-Webb

Duke University, Durham, NC, USA

Purpose: There is a lack of recognition of CTS during stroke recovery, although early literature suggests it is prevalent and inhibits mobility, rehabilitation and recovery. The symptoms of CTS can be difficult to identify in the setting of coexisting neurologic deficits due to stroke. Gold standard electrodiagnostic testing can be uncomfortable and costly. Median nerve ultrasound (US)is now widely accepted as a useful tool for CTS diagnosis that is painless and inexpensive. In this proposed, prospective pilot study, median nerve US will be used to screen stroke patients for development of CTS during their acute presentation and subsequent recovery.

Study design and Procedures: This single-site study will evaluate the incidence of US-identified CTS in patients following stroke. Patients will be assessed within 72 hours of stroke onset, then at their 1 month and 3 month clinic visits. Subjects will be evaluated using the MRC strength score. Subjects who are hemiplegic (MRC of 0) will be placed into one group. Hemiparetic patients who demonstrate an MRC score of 1 to 4 at one arm will be placed in another group. We will also recruit patients that have monoparesis or monoplegia at one arm will each be placed into separate groups. Investigators will perform a focused neurologic exam including Tinel's and Phalen's test on the extremities.

Patients will undergo median nerve US of bilateral median nerves, performed by trained personnel in the Duke Electromyography Laboratory, where this testing has been offered as a standard service since 2006. Our primary outcome is evidence of CTS on ultrasound, based upon pre-existing laboratory established normative values. Median nerve CSA (cross sectional area) at the distal wrist crease of 10-12mm^2 will be considered at risk for CTS, while values >12mm^2 and a ratio of median nerve CSA at the wrist/median nerve CSA at the forearm of >1.5 are considered consistent with CTS. The presence of intraneural blood flow will also be recorded as normal or increased. All abnormal US results will be referred back to the subject's primary neurologist for management, including if additional electrodiagnostic tests are warranted versus treatment.

Our secondary outcome will be based on change in patient reported functional status. Patients will complete the Boston Carpal Tunnel Questionnaire (BCTQ), a widely-used self-reported functional status and symptom severity scale at baseline and during follow-up visits. Our goal enrollment is 20 patients for each study group for a goal of 80 patients. We anticipate completion of enrollment and preliminary data of hospitalized patients by October 2015.

T25: Comparing Stimulation of Bihemispheric Motor Sites on a Reaching Task in Mild and Severe Arm Impairment After Stroke

Rachael Harrington[1,2], Evan Chan[3], Sambit Mohapatra[1,2], Clinton J. Wutzke[2,5], Amanda K. Rounds[2,4], Dijo Abraham[2], Michelle L. Harris-Love[1,2]

[1]Georgetown University, Washington, DC, USA, [2]Medstar National Rehabilitation Hospital, Washington, DC, USA, [3]Medstar Health Research Institute, Washington, DC, USA, [4]George Mason University, Fairfax, VA, USA, [5]Veterans Affairs, Washington, DC, USA

Stroke affects over 610,000 people in the United States every year and many are left permanently disabled. Chronic poststroke arm impairment is particularly disabling and existing treatments are of limited efficacy. There are sites in each hemisphere that it may be beneficial to "prime" in order to enhance the effects of a subsequently applied rehabilitation treatment . One such region is the dorsal premotor cortex (PMd). Previous research demonstrates that PMd has a role in motor control of the ipsilateral arm, direct ipsilateral and contralateral projections to the spinal cord, and the ability to flexibly compensate for asymmetries in function between hemispheres. The role of PMd in poststroke arm impairment, how it may differ from that of other cortical areas and with severity of poststroke arm impairment is not known. The hypothesis are that nlPMd, not lPMd, has a greater role in recovered reaching function in severe more than mild patients and that nlPMd, but not nlM1, has a greater role in recovered reaching function in severe patients.

30 individuals with (n=15) or without (n=15) active wrist and finger movements after poststroke arm impairment participated in a reaching task. Participants were asked to reach as quickly as possible with the affected arm to one of the targets in response to a visual 'Go' signal. TMS was applied between the 'Go' signal and movement onset. Doublepulse TMS (ISI 25 ms) was delivered to nlM1, nlPMd and lPMd at 120% of the individual's Resting Motor Threshold (RMT) for unaffected biceps.

Change in movement time was greater with TMS applied to nlPMd than to lPMD in the severely impaired but not mildly impaired participants. A trend in the data shows an interaction effect between severity and hemisphere. Within only the severe group, change in movement time was greater with TMS applied to nlPMd but not to nlM1. Data suggest that nlPMd has a greater role in recovered arm reaching in severely impaired patients than lPMd and that this effect is not present in mildly impaired patients. Additionally, data show that this is not an effect of the contralesional hemisphere as a whole, but a site specific effect to nlPMd as shown through comparison with disruption of nlM1. This study evaluates the role of nlPMd in recovery of arm function. The results of this study lay the foundation to explore nlPMd as a potential site for upregulation as an adjuvant to traditional therapy in severe patients after stroke. Identification of sites to enhance rehabilitation outcomes of severe patients are essential as there are no currently validated treatments and longterm disability is costly to both personal quality of life and national health care costs.

T26: A Constrained Motor Connectome Characterizes Post-Stroke Upper Extremity Motor Function

Sue Peters, Katie Wadden, Kathryn Hayward, Jason Neva, Lara Boyd

University of British Columbia, Vancouver, BC, Canada

Purpose: Animal models of stroke have shown that white matter distant from the lesion may impact function. Thus, structural reorganization of both hemispheres post-stroke may contribute to motor function. Multimodal neuroimaging that combines structural and functional measures may provide insight into how the residual whole-brain motor network contributes to functional recovery and learning after stroke better than single regional approaches. This study's purpose was to examine whether: 1) a constrained motor connectome (CMC) derived from a multimodal neuroimaging approach could differentiate between healthy individuals and stroke, and 2) the CMC relates to motor function or impairment.

Methods: All participants underwent diffusion imaging at a 3T magnetic resonance imaging (MRI) centre. A bilateral sensorimotor network mask, created from a functional MRI connectivity analysis in healthy participants during motor task retention test, was used to constrain white matter. The clusters from our functional MRI analysis represent an idealized motor network and were used as seed regions to construct a CMC for each participant. Subsequently, diffusion metrics (tract number, fractional anisotrophy [FA], apparent diffusion coefficient [ADC]) were calculated to characterize the CMC. The Wolf Motor Function (WMF) and Fugl-Meyer (FM) upper extremity tests characterized paretic arm function and impairment, respectively. For the WMF, movement time to complete the 15 items was determined and a task rate was calculated. The WMF was also divided into fine (WMF-f) and gross (WMF-g) motor tasks with separate task rates calculated. A one-way between subjects analysis of variance (ANOVA, $p \leq 0.05$) was performed to compare the effect of group on diffusion metrics. Pearson's correlations were calculated for WMF, FM, and diffusion metrics.

Results: Twenty-nine individuals with stroke (age 65.6±10.7 years, 68.1±66.5 months post-stroke) and 18 healthy individuals were scanned. On average, participants with stroke were moderately impaired (FM 48.0±16.8). The ANOVA revealed significant differences between individuals with stroke and healthy for number of tracts [$F(1,45)=11.67$, $p=0.001$], mean FA [$F(1,45)=17.58$, $p<0.001$], and mean ADC [$F(1,45)=3.93$, $p=0.05$] in the CMC. For individuals with stroke, the nonparetic WMF-f correlated with ADC ($r=-0.41$, $p=0.04$), but not with FA ($r=0.27$, $p=0.18$) or tract number ($r=-0.002$, $p=0.99$). The FM did not correlate with diffusion metrics within the CMC.

Discussion: A bilateral CMC is able to differentiate individuals with stroke from healthy. Additionally, the CMC correlated with motor function but not impairment, which suggests that it may be related to functional motor network recovery. As this CMC reflects a large functional motor network, it may capture the compensatory plasticity thought to be involved in post-stroke recovery of motor function. Applying a constrained motor connectome to the post-stroke brain may provide a biomarker for sensorimotor function. Further, this work lends support to the theory that connectivity between hemispheres is likely important for recovery of function after stroke.

T28: Impact of Motor Practice on Neuromodulation for Stroke Rehabilitation

Caylen White[1,2], Damian Funke[1,2], Crystal Massie[1,2]

[1]Indiana University, Indianapolis, IN, USA, [2]Indiana Center for Advanced Neurorehabilitation, Indianapolis, IN, USA

Neuroplasticity is an important factor for upper-extremity stroke rehabilitation. Recent trends in stroke rehabilitation research have focused on influencing neuroplasticity with neuromodulatory techniques such as repetitive transcranial magnetic stimulation (rTMS) and coupling those with motor practice. However, the amount of neuromodulation achieved with an acute session of motor practice is not fully characterized. The objective of this pilot study was to determine how engaging in motor practice with a similar time sequence as a rTMS intervention influences motor control, dexterity, and neuromodulation. Five survivors of stroke participated in this pilot study with a mean age of 60.4 (range 43-84). Each participant completed a motor practice intervention protocol with their stroke-affected arm and hand including 30 bouts of isometric contractions in a customized wrist device for 6 seconds followed by a 30 second rest. Assessments included force steadiness and electromyography during a wrist extension task, the Box and Block Test (BBT), and transcranial magnetic stimulation (TMS) before and after the intervention. The force steadiness task was two trials of at least 10 seconds at 5, 10, and 20% of the maximum voluntary contraction. The BBT is a measure of dexterity assessed as the number of small blocks moved in a minute. The TMS measures included 12 stimulations each at suprathreshold test stimulus (TS, 116% of resting motor threshold), short-interval intracortical inhibition (SICI), and intracortical facilitation (ICF) with motor evoked potentials (MEP) recorded from the extensor carpi radialis (ECR) and extensor carpi ulnaris (ECU) muscles. Data were analyzed with a paired *t*-test. The variability of force steadiness decreased following the intervention for the 5 and 20% conditions ($p < 0.05$). Muscle activity increased from pre-test to post-test with significant increases during the 10% condition ($p = 0.04$) and a trend during the 5 and 20% conditions ($p = 0.06$, and 0.05, respectively). Participants were able to move significantly more blocks with their stroke-affected hand following the intervention ($p < 0.02$), but no changes were observed with the less-affected hand ($p = 0.3$). TMS data was only collected on three subjects. Two of the subjects had increases in MEP amplitude of the TS only stimulations and all three subjects had more inhibition (SICI). These results suggest that a short intervention of isometric wrist extension can influence motor control, dexterity, and neuromodulation. This demonstrates the importance of better understanding how possible rehabilitation interventions contribute to influencing neuroplasticity and promoting greater functional improvements.

T29: Bilateral vs. Unilateral Therapy for Chronic Stroke Patients with Varying Degrees of Motor Impairment: A Crossover Repeated-Measures Design of Neurophysiologic Response

David Cunningham[1,2], Jayme Knutson[3], Kelsey Potter-Baker[1], Vishwanath Sankarasubramanian[1], Nicole Varnerin[1], Corin Bonnett[1], Thelma Asare[1], Andre Machado[1], Ela Plow[1]

[1]Cleveland Clinic, Cleveland, Ohio, USA, [2]Kent State University, Kent, Ohio, USA, [3]Case Western Reserve University, Cleveland, Ohio, USA

Introduction: For patients with chronic stroke, it is believed excitation of the primary motor cortex of the non-lesioned hemisphere (NLH) exacerbates motor deficits by exaggerating transcallosal inhibitory interactions (TCI) upon the lesioned hemisphere (LH). However, recent evidence suggests the NLH may play a compensatory role in recovery for patients with greater motor impairment. If true, then therapies recruiting the NLH would elicit a more adaptive role of the NLH for recovery. Therefore, we tested the hypothesis that therapy involving the NLH (bilateral) would lower TCI exerted upon the LH compared to therapy only involving the LH (unilateral); an effect that would become more pronounced with increasing impairment.

Methods: In a crossover repeated-measures design, six chronic stroke patients with varying degrees of motor impairment (Fugl-Meyer [clinical measure of motor impairment]: 15 [more impaired] to 59 [less impaired]) underwent a single session each of unilateral and bilateral therapy. We measured excitation of the NLH and TCI it exerts upon the LH using transcranial magnetic stimulation. TMS uses electromagnetic induction to depolarize neurons in the cortex and assesses recruitment of hemispheric output to the muscle as motor evoked potentials and the transcallosal inhibition imposed upon the primary motor cortex.

Results: Overall, bilateral therapy resulted in greater NLH and LH excitability when compared to unilateral therapy (NLH: 15.35 ± 33% vs. -6.81 ± 20.2%; LH: 6.51 ± 25% vs. -14.49 ± 21%, $p < .05$). Further, bilateral therapy resulted in a greater reduction of TCI (-27.9 ± 18.6% vs. -5.16 ± 10.2%, $p < .05$), where the effect was more pronounced in the more impaired patients ($r = .829$, $p < .05$).

Conclusion: Our preliminary results show that bilateral therapy may invoke an adaptive rather than inhibitory influence of the NLH with greater motor impairment. Future work will test whether behavioral outcomes following bilateral therapy is superior to unilateral therapy for patients with greater motor impairment.

T31: Improved Upper Limb Skilled Functional Task Performance is Predicted by Mitigated Spasticity in Response to Intensive Motor Learning Therapy in Chronic Stroke Survivors

Svetlana Pundik[1,2], Jessica McCabe[2], Margaret Skelly[2], Curtis Tatsuoka[1], Janis Daly[3,4]

[1]Case Western Reserve University, Cleveland, OH, USA, [2]Cleveland VA Medical Center, Cleveland, OH, USA, [3]McKnight Brain Institute, University of Florida, Gainesville, FL, USA, [4]Brain Rehabilitation Research Center of Excellence VA Medical Center, Gainesville, FL, USA

Purpose: Spasticity is a significant problem for individuals in the chronic stage after stroke or in other types of central nervous system injury. It causes pain and discomfort, and limits effective voluntary movement. Physical or occupational therapy interventions can decrease spasticity. However, it is still uncertain whether there is a relationship between reduction in spasticity and change in function. The purpose of this study was to establish whether there was a relationship between mitigation of spasticity and gain in complex functional task performance, following intensive upper limb rehabilitation.

Methods: We recruited 80 chronic stroke survivors (>6 months post-stroke) with upper limb motor deficits (Fugl-Meyer mean = 23.8 ± 9) and spasticity. Upper limb motor learning therapy was provided for 5 hours/day, 5 days/week for 12 weeks and included progressed practice of functional tasks and their components. Outcome measures were collected before and after rehabilitation and included: modified Ashworth scale (mASH); mASH for wrist/hand muscles (mASH W/H); Arm Motor Ability test, function domain (AMAT-F); and AMAT-F wrist/hand (AMAT-F W/H). mASH was obtained and summed for nine muscles of the upper limb: shoulder internal rotators, elbow flexors and extensors; forearm pronator and supinators, and wrist and digit flexors and extensors. Pre- vs post-rehabilitation scores were compared with Wilcoxon Signed Rank Test. We conducted regression analysis to determine the effect of spasticity mitigation in response to treatment on recovery of functional task performance.

Results: Subjects were 57.6±11.9 years old, 31.4±23.4 months after stroke and 33.7% were female. Following rehabilitation, summated AMAT-F score for whole arm improved from 87±33 to 110±39 ($p<0.001$); AMAT-F W/H improved from 25±15 to 33±17 ($p < 0.001$); mASH improved from 8.5±3.6 to 6.1±3.3 ($p<0.001$). After adjusting for age and baseline AMAT-F W/H score, improved spasticity predicted gain in AMAT-F W/H (parameter estimate coefficient, $\beta = 0.31$ ($p=0.009$)). In exploratory analysis, we found first, that mitigated mASH in digit flexor muscles significantly predicted AMAT-F W/H gain (parameter estimate coefficient $\beta = 0.3$ ($p=0.01$)). Second, we found that mitigated mASH in wrist flexors ($\beta = 0.27$ ($p=0.02$)) predicted improvement of the AMAT-F overall score for the whole arm performance.

Conclusion: Intensive motor learning for the upper limb mitigates abnormal muscle tone. Furthermore, there is a significant relationship between mitigation of spasticity and gain in motor function for upper extremity. Specifically, reduced spasticity in distal arm muscles, i.e. digit and wrist flexors predicted gains in skilled functional tasks, for the wrist/hand components of those tasks.

T32: Contralaterally Controlled Functional Electrical Stimulation and Hand Therapy Video Games for Cerebral Palsy

Michael Fu[1,2], Anna Curby[3], Ryan Suder[3], John Chae[2,4], Jayme Knutson[2,4]

[1]*Case Western Reserve University, Cleveland, OH, USA,* [2]*Cleveland FES Center of Excellence, Cleveland, OH, USA,* [3]*Cleveland Clinic Children's Hospital for Rehabilitation, Cleveland, OH, USA,* [4]*MetroHealth Rehabilitation Institute of Ohio, Cleveland OH, USA*

Purpose: We describe a novel intervention for children with upper extremity hemiplegia due to cerebral palsy.

Intervention: Our home-based intervention integrates a novel electrical stimulation approach with custom video games.

Contralaterally Controlled Functional Electrical Stimulation (CCFES) is a unique form of neuromuscular electrical stimulation that allows children to control the timing and amount of hand opening. A sensor glove is worn on the unimpaired hand that proportionally controls stimulation to surface electrodes on the extensors of the paretic hand. Stimulation is configured so that paretic hand opening mirrors that of the unimpaired hand. This allows children to use CCFES to assist their paretic hand while playing video games.

We developed four hand therapy video games that are controlled by impaired hand opening/closing. Each game trains different motor skills and is designed to engage children in goal-oriented training that require motor planning, control, and concentration.

Paddle Ball trains control of graded hand opening. A paddle's vertical position is controlled by hand aperture. Difficulty is adjusted by changing paddle size and ball speed. Performance feedback is provided by score, hit rate, and motor repetitions.

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

Marble Maze trains maintenance of hand opening. Players rotate mazes to guide marbles out - often needing to hold the maze still while marbles roll. Maze rotation is proportional to hand opening angle. Difficulty is adjusted by bucket size and adding concurrent marbles. Performance is provided by completion time.

Sound Tracker trains continuous precise hand opening. Players control a cursor's vertical motion with hand opening/closing to follow a path generated by a series of songs. Difficulty is adjusted by track width and new songs are presented with 90% accuracy. Performance feedback is provided by accuracy.

Feasibility Study: We have an ongoing feasibility study to establish a protocol for administering the treatment and to estimate its effect on hand impairment and function. The period is 6 weeks, which consists of therapist-guided sessions in lab and self-administered sessions at home. Weekly lab sessions consist of 45 min of CCFES-mediated video games and 45 minutes of CCFES-mediated functional task practice. Daily home sessions consist of 90 mins CCFES-mediated video games.

T33: Connections Between Posterior Parietal and Sensorimotor Cortices Predict Postural Adaptation in People with Multiple Sclerosis

Eline Zeeboer[1], Geetanjali Gera Dutta[1], Heather Schlueter[1], Fay B. Horak[1,2], Brett W. Fling[1]

[1]*Oregon Health & Science University, Portland, Oregon, USA,* [2]*VA Portland Healthcare System, Portland, Oregon, USA*

Introduction: People with Multiple Sclerosis (PwMS) have increasingly well-characterized deficits in gait and balance. As yet, rehabilitation strategies to improve these deficits have limited effectiveness. Studies suggest that PwMS can learn upper limb motor skills; however, it is unknown whether PwMS are able to improve their responses to postural perturbations. Therefore, the first aim of this study was to assess short- and long-term postural motor adaptation in PwMS and healthy controls (HC). The second aim was to identify neuroanatomic networks underlying short- and long-term adaptation of postural responses within PwMS.

Methods: 24 patients with relapsing-remitting MS and 14 age-matched HC stood on a platform that translated horizontally forward and backward, eliciting postural perturbations in the opposite direction. Testing on the first day consisted of five blocks of trials with rest periods between blocks. To separate temporary performance effects from more permanent changes in behavior, participants returned on a second day to assess long-term adaptation. Performance on the perturbation platform was assessed as the relative phase lag of the body center of mass relative to platform motion. Diffusion weighted images (DTI) were also acquired and whole brain tract-based spatial statistics (TBSS) were used to identify associations between white matter microstructural integrity and postural adaptation.

Results: Despite significant deficits in postural motor performance at baseline related to the relative phase measure in PwMS ($P < 0.01$), they demonstrated a similar ability to improve postural control with training compared to HC. TBSS analysis revealed a widespread network of decreased white matter microstructure in PwMS compared to HC, with specific deficits noted in the corpus callosum. Further, TBSS correlation analysis revealed strong associations between short-term adaptation and fiber tract quality within the corpus callosum (genu, body and splenium) as well as white matter tracts connecting the posterior parietal cortices with the primary somatosensory and motor cortices, principally within the left hemisphere ($P \leq 0.05$; corrected for age, brain volume & EDSS). These neuro-behavioral relationships were strongly driven by PwMS.

Conclusions: PwMS have the capacity to improve the use of a feed-forward postural strategy with practice and retain the learned behavior despite their significant postural response impairments. Further, we show that interhemispheric callosal connections and those connecting the posterior parietal cortices with the sensorimotor cortices are strongly related to a given individual's ability to adapt their behavior. The posterior parietal cortex plays an integral role in voluntary movements by assessing the context in which they are being made and integrating somatosensory and visual inputs to determine positions of the body in space. It thereby produces internal models of the movement to be made, suggesting that PwMS who are able to engage this circuitry to a greater extent may benefit more from gait and balance training.

T34: Activation Training Alters Corticomotor Excitability of the Gluteus Maximus

Yi-Ling Kuo[1], Christopher Powers[1], Anna Southam[1], Ya-Yun Lee[1,2], Beth Fisher[1]

[1]University of Southern California, Division of Biokinesiology and Physical Therapy, Los Angeles, USA, [2]Healthy Aging Center, Chang Gung University, Taoyuan, Taiwan

Objectives: To determine whether a short term (6 hours) activation training program targeting gluteus maximus (GM) results in neuroplastic changes in the primary motor cortex (M1).

Study Design: Within subject - repeated measures

Background: It has been proposed that strengthening and skill training of GM may be beneficial in treating various knee injuries. Given the redundancy of the hip musculature and the small representational area of GM in M1, learning to activate this muscle prior to prescribing strength exercises and modifying movement strategy would appear to be important.

Methods: Using Transcranial magnetic stimulation (TMS), motor evoked potentials (MEPs) were obtained in 12 healthy individuals at 5 different stimulation intensities while they performed a double-leg bridge. Participants then completed a home exercise program for approximately 1 hour/day for 6 days that consisted of a single exercise designed to selectively target GM. Baseline and post-training input-output curves (IOCs) were generated by graphing average MEP amplitudes and cortical silent period (CSP) durations against corresponding stimulation intensities. Linear slopes of the IOCs were compared pre and post training using a paired t-test.

Results: Following GM activation training, the linear slope of the MEP IOC increased from 14.89 to 21.51 ($p = .01$). For CSP duration, the linear slope of the IOC increased from 13.74 to 22.64 ($p = .04$).

Conclusion: Short term GM activation training resulted in a significant increase in corticomotor excitability as well as changes in inhibitory processes of GM. We propose that the observed corticomotor plasticity will allow for better utilization of GM in the more advanced stages of a rehabilitation/training program.

Key words: transcranial magnetic stimulation, motor-evoked potential, recruitment efficiency, cortical silent period, inhibition

T35: Methodological Study to Identify Trunk and Hip Muscle Representation in Motor Cortex

Alaa Albishi, Jo Armour Smith, Beth Fisher

usc, los Angeles/ CA, USA

Background: Trunk and hip muscles contribute significantly to postural control, balance and locomotion. With aging, changes in activities of these muscles are evident. While modifications in motor behavior are linked to altered muscle representational areas in motor cortex, the relationship between motor cortex organization of the trunk and hip muscles and changes in motor behavior in older adults has yet to be established. Transcranial Magnetic Stimulation (TMS) has been used to identify muscle representation in the motor cortex. Mapping the trunk and hip muscles is challenging due to the small representations of these muscles in the medial motor cortex.

Purpose: Establish a methodology to quantify the spatial representation of trunk and hip musculature in young and older adults.

Method: Six young females participated in the study. Motor evoked potentials (MEPs) were quantified in the external oblique (EO), lumber longissimus (LES) and gluteus medius (GEMD) using a double cone coil and surface electromyography. After, motor thresholding, mapping of a 6 by 4cm grid over the pre-central gyrus was conducted using neuronavigation during a submaximal active contraction (20% of maximum voluntary isometric contraction) for all three muscles. Average peak-to-peak amplitude of MEPs was calculated for each map location and utilized to determine the center of gravity (COG) for each muscle.

Results: MEPs were elicited consistently in all three muscles. The average COG for GMED was medial to that of LES and EO. COG for all three muscles was localized within primary motor cortex (approximate x, y, z coordinates; GMED 12, -17, 63mm, LES 15, -17, 63mm, EO 14, -17, 63mm in Tailarach space). However, in some individuals the caudal supplementary motor area also contributed significantly to the motor maps.

Conclusion: Initial data demonstrate that this methodology is feasible and can identify distinct trunk and hip representations in the motor cortex.

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T36: The Efficacy of Wii-Based Movement Therapy Upper-Limb Rehabilitation in Chronic Stroke is Accompanied by Ancillary Cardiovascular Benefits

Penelope McNulty[1,2], Angelica Thompson-Butel[1,2], Terry Trinh[1,2], Steven Faux[2,3], Gaven Lin[1], Christine Shiner[1,2]

[1]Neuroscience Research Australia, Sydney, NSW, Australia, [2]UNSW Australia, Sydney, NSW, Australia, [3]St Vincent's Hospital, Sydney, NSW, Australia

Financial constraints in the health sector make the search for more effective and efficient post-stroke rehabilitation more urgent. Wii-based Movement Therapy (WMT) uses the Nintendo Wii and Wii Sports as a tool in a structured 14-day rehabilitation program that targets movement quality of the more-affected upper-limb and increased independence in activities of daily living. We compared dose-matched trials of Wii-based Movement Therapy (WMT) and modified Constraint-induced Movement Therapy (mCIMT) in two studies, i) an assessor-blinded randomised controlled trial of upper-limb therapy efficacy with 42 patients 2-46 months post-stroke; and ii) a post hoc analysis of the cardiovascular benefits of therapy in 46 patients receiving either WMT (n=29) or mCIMT (n=17) from 3-264 months post-stroke (mean 34.8±9.3 months) of whom 28 were studied during the RCT. Primary outcome measures for the RCT were the Wolf Motor Function Test timed-tasks (WMFT-tt) and Motor Activity Log Quality of Movement scale (MALQOM) assessed at pre-baseline (14-days pre-therapy), baseline, post-therapy, and 6-month follow-up. Patients in the cardiovascular study were assessed in the same way with the addition of peak heart rate (HRpeak) and heart rate recovery (HRR) measured during therapy sessions at early (day 2) and late (~day 13) therapy. There were no adverse events. For the RCT there were no differences at any time point between groups for the primary outcome measures. Motor-function was stable between pre-baseline and baseline assessments ($p>0.05$); improved with therapy between baseline and post-therapy ($p<0.001$); and these improvements were sustained at 6 months ($p>0.05$). WMFT-tt log times improved from 2.1 (1.5-2.7) to 1.7 (1.1-2.3) s after WMT and 2.6 (1.9-3.2) to 2.3 (1.7-3.0) s after mCIMT. MALQOM scores improved from 67.7 (51.1-84.4) to 102.4 (84.4-120.3) and from 64.1 (43.6-84.5) to 93.0 (76.5-109.5), respectively (mean, 95% confidence intervals). HRpeak was higher during mCIMT than WMT, but increased by late-therapy only for the WMT group ($p<0.001$). Similarly, HRR was always faster for mCIMT but changed significantly by later-therapy only for the WMT group ($p=0.037$). These data suggest that WMT provides a cardiovascular challenge that improves the cardiovascular fitness of stroke patients in the chronic phase whereas mCIMT induces a cardiovascular stress response. Patient preference and acceptance for WMT were higher than mCIMT with higher levels of sustained therapeutic activities at 6 months. Patients in the WMT cohort reported fewer falls, and greater levels of physical activity and social engagement at 6 months. This study demonstrates that WMT is as effective as mCIMT for upper-limb rehabilitation and increased independence in everyday life but WMT alone confers a cardiovascular benefit. WMT can be implemented across a broad spectrum of post-stroke impairment to provide prolonged therapy intensity and increased physical activity.

T37: Optimal Timing for Combined Neuromodulation Techniques to Enhance Motor Training in Chronic Stroke with Severe Motor Deficit

Elizabeth Powell[1], Cheryl Carrico[1], Kenneth Chelette[1], Laurie Nichols[1,2], Emily Salyers[1], Lakshmi Reddy[2], Lumy Sawaki[1,2]

[1]University of Kentucky, Lexington, KY, USA, [2]Cardinal Hill Rehabilitation Hospital, Lexington, KY, USA

Peripheral nerve stimulation (PNS) and transcranial direct current stimulation (tDCS) are neuromodulation techniques that can increase neuroplasticity and aid in motor recovery after stroke. Only a few studies to date have investigated the effects that tDCS combined with PNS has on outcomes of motor training after stroke. In these studies, the tDCS protocol overlapped with the end of each PNS session. It is conceivable that delivering tDCS at the start (rather than the end) of a PNS session would enhance the effects of PNS. Alternatively, delivering tDCS at the end of PNS could be optimal due to motor training taking place while the motor cortex is still depolarized from tDCS. Because no studies have investigated alternate timing configurations of tDCS combined with PNS, we conducted a proof-of-concept study in which subjects with severe post-stroke hemiparesis received 2 hours of PNS and 20 minutes of anodal tDCS concurrently. tDCS was delivered according to 1 of 2 timing configurations: 1) during the first 20 minutes of PNS ("Start" group; n=4); or 2) during the last 20 minutes of PNS ("End" group; n=6). All subjects received 2 hours of robotic-assisted upper extremity motor training immediately following stimulation. We hypothesized that the "Start" group would have greater improvements in motor function than the "End" group. Outcome measures, taken 1-7 days before starting interventions, and again at 1-7 days after completing interventions, included the upper extremity motor score of Fugl-Meyer Assessment (FMA), Stroke Impact Scale (SIS), and cortical map volume as measured by transcranial magnetic stimulation. We analyzed data using an independent sample t-test. Results indicated modest improvements in FMA for both groups, with slightly greater improvements in the Start group. Though SIS scores improved in both groups, there was a trend towards significantly greater improvement for the Start group compared with the End group ($p=0.062$). Cortical map volume for both hemispheres decreased in the End group, while both increased slightly in the Start group. These results suggest that delivery of tDCS at the start of PNS offers more benefit than tDCS at the end of PNS. A possible explanation is that tDCS at the end of PNS overstimulates the cortex, thus negating potentially therapeutic effects of neuromodulatory intervention. A larger study is needed to substantiate these preliminary results.

T38: Biomarkers of Stroke Recovery Study (BIOREC) Methodology

Matthew Edwardson[1,2], Shashwati Geed[2], Amrita Cheema[1], Ming Tan[1], Barbara Bregman[1,2], Alexander Dromerick[2,1]

[1]Georgetown University, Washington, DC, USA, [2]National Rehabilitation Hospital, Washington, DC, USA

Efforts to improve recovery from stroke are currently limited by a poor understanding of neural injury and repair mechanisms in humans. Here we describe the methodology for the Biomarkers of Stroke Recovery Study (BIOREC), designed to identify potential molecular markers of neural injury and repair in humans. In this pilot study, we capitalize on recent advances in the field of metabolomics to gain a window into neural remodeling after stroke. These advances have made it possible to accurately detect tiny metabolites, many of which pass through an intact blood-brain-barrier. Subjects in BIOREC undergo blood draws at 5, 15, and 30 days post-stroke - a time period during which the majority of neural recovery occurs based on stroke recovery curves. We also carefully measure functional recovery at 5, 15, 30, and 90 days post-stroke using tests of motor, speech, and cognitive abilities. Motor testing includes the upper extremity Fugl-Meyer (UE-FM), nine-hole peg test, and kinematics using the Zebris 3D-motion detector. Inclusion criteria, which are strict to reduce blood sample variability, include ischemic middle cerebral artery stroke larger than 25cc on neuroimaging, age 50-70, pre-stroke mRS < 2, and presumed cardioembolic source. BIOREC recently received IRB approval and will start recruitment at MedStar Georgetown University Hospital and MedStar Washington Hospital Center in Washington, DC. We anticipate 1 year to reach our recruitment goal of 24 stroke patients and an equal number of age-matched controls. Blood samples will be analyzed at study conclusion. BIOREC will identify novel metabolites that have a different concentration in the blood of stroke patients in comparison to age-matched controls. We suspect that metabolite changes detected early after stroke (day 5) will primarily reflect neural injury, while those detected late (day 15, 30) will reflect neural repair. This hypothesis will be tested in a larger follow up study aimed at linking specific metabolite changes with good and poor recovery using UE-FM as the primary outcome measure. This work was supported by grant 1U10NS086513-01.

T39: Investigating Dynamics of Motor Evoked Potentials During Isometric Contraction

Michael Dimyan[1,4], Elsa Ermer[1,4], George Wittenberg[1,4]

[1]University of Maryland School of Medicine, Baltimore, MD, USA, [2]University of Maryland Rehabilitation & Orthopedic Institute, Baltimore, MD, USA, [3]University of Maryland Pepper Center, Baltimore, MD, USA, [4]VA Maryland Health Care System, Baltimore, MD, USA

The amplitude of muscle potentials evoked by transcranial magnetic stimulation is often used to describe the overall state of the corticomotorneuronal system. Paired-pulse stimulation evokes potentials that allow exploration of inhibitory effects on motor cortical effectiveness. In order to tease out the effect of a behavioral condition on paired-pulse evoked potentials, it then becomes necessary to attempt to adjust for the effects of the behavior on the test and conditioning evoked activity separately. This is most often done by adjusting the stimulation intensity to match motor evoked potential amplitudes across behavioral conditions. While this method of adjustment is well established, it is limited by the presumption that the behavioral condition, such as voluntary muscle contraction, has linearly correlated effects on test and condition evoked potentials. It may also be practically difficult to match stimulus responses across non-linear recruitment curves. To overcome this limitation, we have developed a method by which a recruitment curve across stimulation intensities for one muscle is defined first, and then paired pulses are applied across stimulation intensities for both conditioning and test evoked potentials. These recruitment curves, taken at both rest and during isometric muscle contraction, can be compared, controlling for respective changes in evoked potentials and behavioral condition. This method allows us explore the dynamics of interhemispheric inhibition during unimanual isometric muscle contraction.

T40: Intensive Home-Based Prism Adaptation Treatment for Chronic Spatial Neglect: A Case Study with Bilateral Lesions

Peii Chen, Meghan Caulfield

Kessler Foundation, West Orange, New Jersey, USA

Prism adaptation is a visuomotor phenomenon resulting from goal-directed limb movements toward visual stimuli while the entire visual field is shifted by prism lenses. The adaptation requires no top-down strategy and occurs automatically. Since 1990, rehabilitation researchers found prism adaptation a promising approach to treat spatial neglect. With damage primarily in the right hemisphere, affected individuals pay no or incomplete attention to the left side of the space. Candidates for prism adaptation treatment (PAT) are individuals with intact right medial temporal regions and no cerebellar lesion. However, because almost all the previous studies included only individuals with unilateral right brain damage, it is unknown whether PAT is beneficial for individuals with bilateral lesions, and the present study was designed to explore on this question.

In this study, a 69-year-old man with chronic left-sided neglect (34 months post right-brain stroke and 46 months post left-brain stroke) underwent a month-long intensive home-based PAT. The patient's spouse was thoroughly trained to perform two PAT sessions daily on every weekday for four weeks. In the intervention period, we called the patient's spouse weekly, and she kept a daily log recording the activities performed during each 20-min session. We assessed the patient using line bisection, Bells Test, and figure copying repeatedly on 5 consecutive days before and after PAT. In addition to paper-and-pencil outcome measures, we also included Barthel Index (BI) and Kessler Foundation Neglect Assessment Process (KF-NAP), and diffusion tensor imaging (DTI) scans before and after PAT. The patient had extensive lesions in the calcarine sulcus and lingual gyrus in the left hemisphere, and lesions from the middle frontal gyrus to the middle occipital gyrus inclusive of the superior and middle temporal gyrus, insula and caudate in the right hemisphere.

After the PAT, the patient showed improvement in line bisection (rightward bias changed from 24.2±3.4 to 10±4.2 mm, t test: $p = .030$), but not in Bells test ($p = .850$) or figure copying ($p = .152$). His BI scores did not change (60 pre and post-treatment). His KF-NAP scores improved from 14 to 11 but remained in the range of moderate severity. His DTI images, however, showed that diffusion in the posterior region of corona radiata changed from dorsal-ventral to anterior-posterior direction in the left hemisphere.

The present study suggests that PAT may not generate clinically meaningful improvement in individuals who had bilateral brain lesions involving regions as extensive as this case. However, the intensive PAT intervention may lead to structural changes in the relatively intact hemisphere. Further follow-ups are necessary to examine whether such changes persist over time and even promote behavioral changes.

T41: Condition-Specific Deficits in Intersegmental Coordination After Stroke

Krithika Sambasivan[1,2], Katherine Haentjens[3], Sajida Khanafer[4], Sandeep K Subramanian[2,5], Melanie C Banina[2], Anatol G Feldman[5], Heidi Sveistrup[6,7], Mindy F Levin[1,2]

[1]School of Physical and Occupational Therapy, McGill University, Montreal, QC, Canada, [2]Jewish Rehabilitation Hospital, Centre for Interdisciplinary Research in Rehabilitation in Greater Montreal Area (CRIR), Laval, QC, Canada, [3]Bachelor in Neuroscience, McGill University, Montreal, QC, Canada, [4]School of Human Kinetics, University of Ottawa, Ottawa, ON, Canada, [5]Department of Neuroscience, University of Montreal, Montreal, QC, Canada, [6]School of Rehabilitation Sciences, University of Ottawa, Ottawa, ON, Canada, [7]Elisabeth Bruyere Hospital, Ottawa, ON, Canada

Stroke leads to deficits such as weakness, spasticity and incoordination affecting upper-limb reaching. Reaching is also affected by stroke-related postural control problems characterised by an increase in lateral deviations of the centre of pressure (evaluated with Limits of Stability (LoS) index). Deficits in the coordination of a redundant number of degrees-of-freedom (DFs) of the body (excess DFs), may also affect reaching. We characterised reaching ability of both arms, with and without the involvement of additional trunk DFs in patients with chronic stroke (18-75yrs; Fugl-Meyer Assessment (FMA): 54.0±12.5/66; Reaching Performance Scale for Stroke (RPSS): near=15.6±2.9/18; far=15.7±3.0/18 target) and Chedoke Arm and Hand Activity Inventory (CAHAI): 47.4±12.8/63) compared to healthy age-matched controls.

Kinematics of two arm tasks involving a target located at 66% arm length were recorded in seated subjects without vision: stationary-task (maintaining finger above target) and reaching-task, while leaning the trunk forward (total of 40 trials). For each task, in 40% of trials, trunk movement was unexpectedly blocked such that movements were made with and without trunk involvement. LoS in sitting was measured in 8 directions separated by 45° intervals using a force-plate. The primary outcome measures were gain (G) for stationary-task defined as the degree to which the potential contribution of trunk displacement to hand motion was compensated by appropriate changes in arm DFs (G=1: complete compensation, G=0: no compensation); and endpoint position difference in reaching-task. Comparisons were made with Mann-Whitney U tests. Clinical measures and LoS area were correlated with primary outcomes.

G of more-affected arms was lower (G=0.49±0.19) compared to less-affected arms (G=0.69±0.14; U=20.5, p=0.02) and controls (G=0.74±0.16; U=7.00, p=0.04). There was no correlation between the more-affected arm G and FMA, CAHAI, LoS area. Endpoint position differences were similar between groups but those of the more-affected arms correlated with FMA (r=-0.76), RPSS (near: r=-0.85, far: r=-0.87) and LoS area (r=0.71).

Stroke affects the ability to compensate for additional trunk movement when the hand is held stationary. During reaching, excessive trunk movement compensates for deficits in upper limb motor function. Patients with stroke have deficits in condition-specific adjustment of intersegmental coordination. Understanding motor control deficits in managing redundant DFs will help clinicians develop targeted interventions to improve upper limb reaching ability in individuals with stroke.

T42: Temporal and Spatial Upper-Limb Interjoint Coordination in Chronic Stroke Subjects Versus Healthy Individuals When Reaching

Marcos R M Rodrigues[1,2], Matthew Slimovitch[2,4], Andreanne K Blanchette[2,3], Mindy F Levin[1,2]

[1]School of Physical and Occupational Therapy, McGill University, Montreal, QC, Canada, [2]Feil and Oberfeld Research Center, Jewish Rehabilitation Hospital, Center for Interdisciplinary Research in Rehabilitation of the Greater Montreal (CRIR), Laval, QC, Canada, [3]Department of Rehabilitation, Laval University, Quebec, QC, Canada, [4]Faculty of Medicine, McGill University, Montreal, QC, Canada

Movement coordination which plays a major role in upper-limb(UL) functionis commonly affectedafter stroke. We assessed UL interjoint coordination (IJC) deficits in people with stroke compared to age- and gender-matched healthy subjects and the influence of these deficits on the performance of a simple reaching task. UL kinematics were recorded using 28 markers on the arm, trunk, nose and target (Optotrak, 30s, 100Hz). Two trials of 10 movements each in which subjects (n=20) alternatively touched their nose and a target (ReachIn; ReachOut) located at 90% arm-length, as fast as possible were recorded for each arm. Healthy subjects (n=20) made the same reaching movementsat self-paced and slow speeds to match speeds of stroke subjects. Data for movements in each direction were analyzed to determine relationships between time to perform the task and arm and trunk kinematics. The relationships between temporal and spatial IJC kinematic measures and clinical scores were determined. Compared to healthy subjects, stroke subjects made more curved endpoint trajectories (Index of curvature: stroke=1.23, control=1.04, $p < 0.05$, ReachIn) and used less shoulder horizontal abduction (stroke=11.8°, control=17.6°, $p < 0.001$, ReachIn).Stroke subjects moved their affected arm slower than their less-affected arm (ReachIn: 18%, ReachOut: 43%; for both directions F=14.136, $p<0.001$) and had more curved trajectories (ReachIn: 18%, ReachOut: 27%; for both directions F=6.003, $p<0.05$).Interjoint coordination was similar between the two arms. Stroke severity was moderately correlated with endpoint speed (r=-0.55, p=0.006) and straightness (r=-0.47, p=0.018) but not precision. Time to perform the task correlated with endpoint straightness (r=0.77, p=0.001), temporal (r=0.63) and spatial (r=-0.61) interjoint coordination. Shoulder horizontal abduction range (β=0.127), temporal (β=0.855) and spatial (β=-0.191) interjoint coordination explained 82% of the variance in the time to perform the task. Shoulder movement and temporal and spatialinterjoint coordination were predictive of the time to perform the task, indicating the influence of UL joint configuration limitation for the performance of reaching movements after stroke.

T43: Motor Equivalence During Whole Body Reaching In Healthy Young Adults

Yosuke Tomita[1,2], Anatol Feldman[2,3], Mindy Levin[1,2]

[1]McGill University, School of Physical and Occupational Therapy, Montréal, Canada, [2]Center for Interdisciplinary Research in Rehabilitation (CRIR)-Jewish Rehabilitation Hospital, Laval, Canada, [3]Université de Montréal, Département de neuroscience, Montréal, Canada

The large number of kinematic degrees of freedom (DFs) of the body allows tasks to be accomplished using different combinations of DFs (motor equivalence). Despite this redundancy, certain movement features remain invariant. For example, hand trajectory and endpoint precision remained invariant when trunk movement was unexpectedly blocked during reaching from a sitting position. We hypothesized that hand trajectory and endpoint precision may remain invariant regardless of unexpected postural perturbations during whole body reaching from standing, which involves a larger number of DFs. Five healthy young subjects moved the hand to a remembered target located beyond the arm length with their eyes closed during standing (Free-Hip trials; FH). In randomly chosen trials, hip flexion was unexpectedly prevented by an electromagnetic device, forcing the subject to take a step while reaching (Blocked-Hip trials; BH). Reaching movements were also recorded when subjects intentionally made a step (Intentional-Step trials; IS). Upper/lower limb and trunk kinematics and ground reaction forces were recorded. Endpoint trajectory, joint kinematics and shifts in the postural center of pressure were analysed. Reaching trajectories and endpoint precision were invariant between FH and BH trials, while those of IS trials in some subjects differed. Invariance in the endpoint trajectory between FH and BH trials was maintained by changes in elbow/shoulder interjoint coordination patterns which occurred after the time of endpoint peak velocity. Stepping reactions resulting from the perturbation were also initiated after the time of the endpoint peak velocity in BH trials. Thus, unexpected recruitment of additional DFs that challenges postural stability during reaching from a standing position did not affect hand trajectories and endpoint precision. Movement adaptation occurred after the endpoint peak velocity to maintain invariance in endpoint trajectories, confirming our hypothesis that the nervous system can take advantage of the redundancy in the number of DFs to stabilize task performance, resulting in motor equivalence.

T44: Effects of Positioning Exercise On Locomotor Function After Contusive Spinal Cord Injury in Rats

Eseul Song[1,3], Hochung Jeon[1,3], Sunk-Chan Hahm[1,3], Youngkyung Kim[2], Young Wook Yoon[2], Junesun Kim[1,3]

[1]College of health science, Korea University, Seoul, Republic of Korea, [2]Collge of Medicine, Korea University, Seoul, Republic of Korea, [3]Department of Public Health Science, Graduate School of Korea University, Seoul, Republic of Korea

Rehabilitation exercise has been applied to prevent the progress of sensorimotor impairments in patients with spinal cord injury (SCI). In particular, most of all mainly have been focused in the effect of locomotion training. However, the effects of other rehabilitation approaches applied in patients with SCI except for locomotion training are still unclear and thus investigation for additional approaches is needed. Thus, we examined the effects of passive stretching exercise (SE) and positioning training (PT) on recovery of locomotor function. Spinal contusion was made in male Sprague-Dawley rats using NYU impactor on T12 spinal cord under anesthesia. Rats were randomly assigned to SE (n=10), PT (n=9), combined SE and PT (C, n=10) and no exercise (control, n=9). SE applied 6 muscles on hindlimb for 1 minute in each motion alternately side repeated 2 sets. PT held quadripedal posture with plantar contact for 30 min. C performed 1 set of SE and 15 min of PT. These interventions were applied 5days/week for 4weeks. Locomotion recovery was assessed by BBB open field locomotor scale and combined behavior score (CBS). Hypersensitivity after SCI was evaluated by paw withdrawal threshold (PWT) with up - down method. Average, maximum speed and travelled distance that reflect the ability of physical activity were measured by using

Panlab's smart tracking system. Luxor fast blue and cresyl violet staining was used to measure areas of cavities on epicenter.

In the PT group, BBB was significantly increased at 10, 11, 12 and 13 days after SCI, and CBS also significantly decreased at 10, 11 and 12 days after SCI compared to control. BBB and CBS in the PT group slightly increased compared to them in the SE group during intervention.

PWT in the PT group was significantly increased from 18 days to 28 days than it in the control. In all rehabilitation exercise groups, values of physical activities showed increased tendency on chronic stages and then only maximal velocity in the PT group were significantly faster than control group. Areas of epicenter cavity were no difference between each group.

These results suggest that SE was no effect to locomotion recovery whereas PT with manually partial support may be more helpful than SE to recovery of locomotor function and hypersensitivity after SCI. This study suggests positive potential for therapeutic exercise to improve locomotor function in SCI rats, though the more work related with mechanism is still needed. This research was supported by the convergence technology development program for bionic arm through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT& Future Planning (2014M2C1B2048632).

T45: Effects of Transcutaneous Electrical Nerve Stimulation (TENS) on Hand Dexterity in Chronic Acquired Brain Injury

Adelyn Tsu[1,2], Jason Godlove[1,2], Gary Abrams[1,2], Karunesh Ganguly[1,2]

[1]San Francisco VA Medical Center, San Francisco, CA, USA, [2]University of California San Francisco, San Francisco, CA, USA

Background: Few patients recover full functional hand dexterity after an acquired brain injury such as a stroke. Transcutaneous electrical nerve stimulation (TENS) is a low cost, easily accessible, home-based treatment modality that has been associated with improvements in hand motor function.

Objective: To investigate the short-term kinematic and functional changes of the distal upper limb after administration of TENS in individuals with chronic hand dexterity dysfunction caused by acquired brain injury.

Methods: 10 participants with a 6-month or greater history of acquired brain injury and distal upper limb motor impairment received a single two-hour session of submotor/suprasensory threshold TENS applied to the median, ulnar, and radial nerves simultaneously. The primary outcome measure was the Action Research Arm Test (ARAT). Secondary outcome measurements included the Nine Hole Peg Test, measurements of finger fractionation and range of motion, and the modified Ashworth scale (MAS). Assessments were performed pre-intervention, immediately post-intervention, and after a one hour rest period post-intervention.

Results: Peripheral nerve stimulation using a TENS device was associated with significant improvements in the ARAT one hour post-intervention, the MAS immediately post-intervention, in addition to finger fractionation of the index finger and range of motion both immediately and 1 hour post-intervention.

Discussion: Improvement in distal motor upper limb function after TENS, as indicated by the significant improvement in the ARAT, was associated with improvements in spasticity and kinematic measurements of finger dexterity. More specifically, there is evidence to suggest TENS may improve impairments in finger fractionation and range of motion. These results provide a stepping stone to building a much needed and more effective model for long-term rehabilitative paradigms to improve hand dexterity recovery.

T46: Sensorimotor Changes After an Intervention Using a Novel Assistive System – Rein Hand: A Case Report

Jun Yao, Natalia Sanchez, Meriel Owen, Carolina Caramona, Jane Sullivan, Julius Dewald

Northwestern University, Chicago, IL, USA

Purpose: Approximately, 75% of survivors with moderate to severe stroke lose hand function. In order to enable this population to functionally use the paretic hand for reaching/grasping and retrieving/releasing, a newly developed electromyography-triggered neuromuscular electrical stimulation system – ReIn-Hand – was used to assist voluntary hand opening during functional reaching. ReIn-Hand allows for individuals with moderate to severe stroke to participate in an intervention of the paretic hand and arm under functional context for the first time. We examined the effect of ReIn-Hand on voluntary hand opening ability, and associated neural changes in these individuals.

Methods: Two individuals with moderate to severe chronic stroke (S1 and S2) completed 6 weeks of training, 3 times per week. During each session, subjects used the ReIn-Hand to assist the paretic hand opening during 20-30 trials of tasks involving reaching/grasping and retrieving/releasing jars with various sizes and weights.

Electroencephalogram during maximum hand opening with the arm supported on a tabletop or in free space was measured before and after the 6-week intervention. These data were then used to reconstruct the cortical activity during hand opening.

Diffusion tensor images (DTI) were also acquired before and after the 6-week intervention with diffusion weighting of 1000 s/mm^2 in 60 diffusion directions. DTI-tractography was used to reconstruct the corticospinal pathways between the posterior limb of the internal capsule and the cerebral peduncle.

Active range of motion, Chedoke MacMaster Stroke-assessment-hand subscale (CMcM), Semmes-Weinstein Monofilament test, the Nottingham Stereognosis Assessment (NSA) and grip strength were assessed before and after the intervention.

Results: At post-test, both subjects had improved scores on the Semmes-Weinstein Monofilament test (S1 from 4.56 to 4.31, S2 from 3.61 to 2.83) and the NSA (S1 from 4 to 12 out of 20, S2 stayed at 19/20), grip strength (1% in S1 and 10% in S2 increases in 'affected-to-unaffected ratio') and increased voluntary index finger extension at the metacarpal-phalangeal joint (increases in S1 and S2 were 26° and 31°). S2 demonstrated 1-point improvement in CMcM. Increased integrity of the corticospinal tract was observed in both subjects, as demonstrated by an increased ratio of fractional anisotropy (FA), as quantified by $(FA_{lesioned\ side} - FA_{nonlesioned\ side})/(FA_{lesioned\ side} + FA_{nonlesioned\ side})$ (increases in S1 and S2 were 0.33% and 3.86%), which was associated with an increased cortical activity from contralateral M1 area at post-test compared to pre-test cortical activity.

Conclusions: These preliminary results suggest that using the ReIn-Hand during functional reach/grasp training may be able to improve voluntary hand control and sensory perception and improve the integrity of the corticospinal tract from the lesioned hemisphere in individuals with moderate to severe chronic stroke. Further investigation in a larger population is needed to evaluate the effectiveness of the ReIn-Hand system.

T47: Different Levels of Intracortical Inhibition are Involved in Bimanual Common vs. Dual-Goal Tasks and Related to Interlimb Interaction

Wan-Wen Liao[1], Jill Whitall[1,2], Joseph Barton[1,3], Sandy McCombe-Waller[1]

[1]Department of Physical Therapy and Rehabilitation Science, School of Medicine, University of Maryland, Baltimore, MD, USA, [2]Faculty of Health Sciences, Southampton, UK, [3]Department of Neurology, School of Medicine, University of Maryland, Baltimore, MD, USA

Individuals following stroke have exhibited various degrees of deficits in both paretic and non-paretic arms. Nevertheless, the majority of activities of daily living require collaboration between the arms. Some tasks involve a common-goal in which two arms sharing a single focus, such as pulling out a drawer with both arms. Others involve similar but separate goals for each arm, such as picking up different items with each arm separately. The ability to restore function of both arms in bimanual tasks is crucial for stroke survivors to achieve independent living. We hypothesize that different cortical control parameters are involved in bimanual common versus dual-goal tasks, and that this difference will be demonstrated in interlimb performance interaction as well. In this pilot we determine intracortical inhibition and its relationship to interlimb interaction in bimanual common-goal vs. dual-goal isometric force tasks in young non-disabled adults.

Subjects: Eight right-handed subjects.

Methods: Isometric force tasks with visual feedback were undertaken in three conditions: unimanual, bimanual dual goals for each arm and bimanual common-goal for both arms. Force production of each arm during 10% submaximal tasks and intracortical inhibition (SICI) of both hemispheres for biceps were evaluated during the three conditions.

Results: A significant reduction of SICI was found in both bimanual tasks compared to the unimanual tasks ($p<.05$) in dominant hemispheres, with a trend toward greater reduction in dual-than common-goal tasks ($p=.06$). Both bimanual tasks showed less intracortical inhibition compared to unimanual tasks in non-dominant hemispheres, but only dual-goal tasks reach a statistically significant difference ($p<.05$). A significant relationship was found between the difference of force variability of each arm and total motor output (the sum of force during bimanual contractions) in common but not dual-goal tasks based on a linear regression model ($p<.05$, $R^2= .805$).

Conclusion: Bimanual common and dual-goal tasks could release both hemispheres from mutual inhibition. The levels of SICI within and between hemispheres as well as force organization pattern were different in common- vs. dual-goal tasks, and this may suggest that these two tasks were modulated by potentially different inhibitory cortical parameters. Our findings indicate that task specific training might be needed for different types of bimanual tasks in healthy as well as patients with neurological disorder.

T49: Navigated Repetitive Transcranial Magnetic Stimulation of Pre-Supplementary Motor Area on Fronto Basal Ganglia Network to Treat Frontal Lobe Stereotypy Following Traumatic Brain Injury : A Case Report

Hoo Young Lee, Tae Woo Kim, Yoon Tae Kim, Soon Hyun Lee, Sang Kyu Shin

National Traffic Rehabilitation Hospital, Catholic Medical Center, Gyeonggi-do, Republic of Korea

Introduction: Pre-supplementary motor area (SMA) has a critical role in response inhibition and control of stopping through fronto basal ganglia network. To date, the use of repetitive transcranial magnetic stimulation (rTMS) of pre-SMA to treat frontal lobe stereotypy after traumatic brain injury (TBI) has not been reported. Here we describe the first successful therapeutic effect of navigated rTMS in the treatment of proximal motor stereotypy.

Case: A 23 year-old patient who was diagnosed quadriplegia due to intracerebral hemorrhage in both frontal lobes, traumatic subdural hemorrhage in left frontotemporal area, and diffuse axonal injury was admitted. She showed anteroposterior axial body rocking and symmetric movement of both shoulders, elbows, and hips that repeated in the same form continuously for long periods of time. The movement disorder was diagnosed as frontal lobe stereotypy at the neurology consultation. Electroencephalography showed no ictal waves. It was refractory to medication such as clonazepam and buspirone.

Paracentral and cingulate sulcus depicted in high resolution T1-weighted MRI scan of the patient were used as landmark for target area of navigated rTMS. She recieved 10 sessions of 10 Hz rTMS at both pre-supplementary motor area over 2-week period at 90% of resting motor threshold. Functional reach test and balance test by measurement of the weight distribution index (WDI) using the BioRescue were performed immediately after each rTMS session. Due to stereotypy-induced poor balance, functional reach test and WDI of ischial tuberosity was evaluated in a independently sitting position.

The patient showed improvement in the functional reach test in both arms. At first, WDI was unmeasurable due to poor sitting balance. But at the last session, WDI was improved to 85%.

Conclusion: This case report suggests that rTMS of pre-SMA may improve frontal lobe proximal motor stereotypy by affecting fronto basal ganglia network. Pilot studies to further evaluate the effectiveness of rTMS of pre-SMA on stereotypy warrant consideration.

T50: Corticospinal Resetting of the Threshold (Referent) Position for Activation of Muscles During Motion at the Elbow Joint

Sandeep Subramanian[1,6], Laetitia Rodrigues[2,6], Louis Ryckembusch[2,6], Tara Brohman[3,6], Dorothy Barthelemy[4,6], Mindy Levin[5,6], Anatol Feldman[1,6]

[1]Neurosciences, Univ. De Montréal, Montreal, Quebec, Canada, [2]Biomed. Engin., Univ. Paris Descartes, Paris, France, [3]Inst. de génie biomédical, Univ. de Montréal, Montreal, Quebec, Canada, [4]École de réadaptation, Univ. De Montréal, Montreal, Quebec, Canada, [5]Sch. of Physical and Occup. Therapy, McGill University, Montreal, Quebec, Canada, [6]Ctr. for Interdisciplinary Res. in Rehabil. of Greater Montreal (CRIR), Montreal, Quebec, Canada

Muscles become active when the actual position of body segments deviates from their threshold positions. Threshold positions represent the origin of the spatial frame of reference (FR) for muscle action. The level of muscle activity depends on the difference between the actual and threshold body segment positions. Voluntary motor actions result from central shifts in the threshold position, thus shifting the FR. It has been shown that the corticospinal (CS) system is involved in threshold position resetting underlying motion at the wrist joint. We investigated whether or not the CS system accomplishes threshold position resetting at the elbow joint. We also investigated how injury affecting the CS tract influences threshold position resetting. Subjects with upper limb hemiparesis after stroke (Fugl-Meyer scores: 20-65/66) and two groups of healthy controls (young: aged 20-35) and older (age-matched to the stroke group) participated in the study. All subjects voluntarily moved their elbow joint from an initial flexed to a final extended position and vice-versa for a total of 30 trials. CS influences at both positions were measured using MEPs elicited by transcranial magnetic stimulation to the biceps site in the contralateral motor cortex. Passive elbow muscle forces were compensated with an elastic band such that elbow muscle activity was approximately equalized at the two positions. Muscle activity was recorded from two elbow flexors (biceps brachii and brachioradialis) and extensors (lateral and medial heads of triceps brachii). Although the EMG activity of elbow muscles was similar, CS influences were different at the two positions. In the healthy groups, flexor MEPs were greater in the elbow flexion than the extension position and vice versa for extensors (reciprocal pattern). Similar patterns were observed only in a subgroup of patients. In the remaining patients, the pattern was either absent or reversed. Results support the notion that CS system participates in threshold position resetting underlying active motion and that this capacity may be affected by stroke. Results also reinforce previous findings suggesting that the motor cortex controls motor actions by shifting spatial FRs. Deficits in shifting spatial FRs may underlie motor deficits in stroke.

T52: Quantifying Post-Stroke Apathy with Actimeters

Andrew Goldfine[1], Behdad Dehbandi[2], Juliana Kennedy[2], Briana Sabot[2], Cory Semper[2], David Putrino[2]

[1]Stony Brook Medicine, Stony Brook, NY, USA, [2]Burke Medical Research Institute, White Plains, NY, USA

Post-stroke apathy is a syndrome of reduced goal-directed behavior and flattening of emotions that occurs in approximately 35% of patients after stroke, and is associated with slower recovery and more disability. There are no proven treatments, and clinical trials are hampered by a lack of objective quantification of apathy severity. Here we tested the hypothesis that amount of spontaneous movement can serve as a quantifiable measure of apathy severity. We studied 57 patients admitted to an acute rehabilitation unit for ischemic or hemorrhagic stroke; all had intact strength on one side, and none had a neurodegenerative movement disorder or were hypoaroused. Spontaneous movement was measured using actimeters (wrist-watch style accelerometers) attached to the wrist of subjects' full strength arm for over 24 hours. Apathy was scored by the treating speech pathologists using the Apathy Inventory (AI; scores range 0-12 with 0 no apathy and 12 persistent and severe apathy). Using a threshold of 4 for defining clinically significant apathy, 21 (36%) of subjects had apathy. Apathetic subjects were well matched to non-apathetic subjects by age, though were typically weaker and more disabled from their stroke. We used multiple linear regression to determine the association between total movement between 9AM and 5PM and multiple predictors. We found that after accounting for motor deficit (Fugl-Meyer of the affected arm) and age, each increment of AI score correlated with 5.6 fewer minutes moving per hour ($p<0.001$). Motor deficit correlated weakly with minutes moving per hour ($p=0.04$), and age did not correlate ($p=0.2$). As a control analysis, we looked at movement while asleep and found no correlation between AI score and minutes moving per hour ($p=0.93$). Our results suggest that wrist worn actimeters may serve as an objective, quantifiable measure of post-stroke apathy in patients with an intact upper extremity. Before they can be used as a clinical trial outcome measure, we need a longitudinal study to determine their responsiveness to change in apathy severity within subjects.

T53: Effect of Creatine Supplementation on Cognition During Hypoxia in Mild Traumatic Brain Injury

Clare Turner, Winston Byblow, Suzanne Barker-Collo, Robert Kydd, Nicholas Gant

Centre for Brain Research, The University of Auckland, Auckland, New Zealand

The brain relies on an uninterrupted supply of oxygen in order to function optimally. Dysfunctional oxidative metabolism occurs with many neurological conditions, including mild traumatic brain injury (mTBI). Creatine is a compound that replenishes cellular energy without oxygen and can be administered as a dietary supplement. Creatine is capable of improving cognitive functions during oxygen deprivation[1]and may have similar effects for those recovering from mTBI.

The aim of this study was to assess the effects of dietary creatine monohydrate supplementation on brain creatine and cognitive functions after mTBI. Spectroscopy was used to measure neural creatine availability. Neuropsychological assessments were conducted during a hypoxia protocol that induces cognitive impairments similar to those experienced after mTBI[2]. Neuropsychological function was measured at baseline and following 7 days of dietary creatine supplementation during the hypoxia intervention.

Participants adhered to the 7 day supplementation regime, confirmed by an 8% increase in creatine within sensorimotor cortex. Creatine improved hypoxia-induced impairments in a range of cognitive domains scores that are commonly impaired following mild TBI. Verbal, visual and composite memory domains, psychomotor speed, and an overall neurocognitive index appear to be protected from oxygen deprivation by creatine supplementation. An enhanced energy-buffering capacity associated with augmented neural creatine stores likely increases energy provision in metabolically-vulnerable brain tissue. These preclinical findings suggest that creatine has utility to improve brain function in patients recovering from mTBI.

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T54: Assessment of Executive Function in Acute Rehabilitation Inpatients Using Hands-Free Cognitive Tests

Avantika Naidu, Victor Mark, Byron Lai

University of Alabama at Birmingham(UAB), ALABAMA, USA

Background: Rehabilitation during acute inpatient hospitalization is highly influenced by executive functions (EF). The role of EF in governing functional independence is well known. However, the development of an EF battery that can accommodate acute disability is challenging. One limitation is that many EF assessments require intact hand control (e.g., Trail Making Test [TMT], Wisconsin Card Sort); thus the EF capabilities of patients with manually disabling disorders remain infrequently investigated. Furthermore, patients admitted to acute rehabilitation for limb disability are also vulnerable to cognitive impairment, even in the absence of acute brain illness (Woods AJ et al., PM&R 2011). In addition, the limited availability of hands-free EF assessments limits understanding of whether EF may be important for disabled individuals to learn new hands-free technologies.

Objective: The purpose of this study was to establish feasibility in evaluating EF by administering a novel brief hands-free battery of tests in the acute rehabilitation environment and sensitivity to acute illness relative to healthy community-living adults.

Methods: A convenience sample of 50 individuals participated in the study. Subjects were required to be alert, attentive, able to comprehend adult-level English well according to clinical judgment, and have sufficient visual acuity to comprehend the consent form at a comfortable reading distance. Experimental group consisted of patients in an acute rehabilitation hospital with and without known brain injury (n=33) and non-impaired community-dwelling adults (n=17). Both groups were administered a battery of three hands-free EF tests: (1) NIH Examiner anti-saccades test (ability to gaze in the same side (pro-saccade) and to the opposite side (anti-saccade 1 & 2) of a randomly appearing dot on-screen); (2) Controlled Oral Word Association Test (COWAT) (total unique words starting with either F, A, or S in 60 sec each); and (3) a novel computer-assisted oral TMT (trails were automatically generated on a computer screen as the subject reported the ascending order and color of numbers and letters; outcome was time to completion for TMT baseline, TMT1 & TMT2).

Results: All subjects completed the EF assessment in one session. Patients and controls did not differ in age or years of education (p's>0.05). Assessment scores were compared between the groups using independent sample t-tests, significant differences were seen for TMT baseline (p=0.01), TMT1 (p=0.03), TMT2 (p=0.02) and anti-saccade trial (p=0.01). No significant differences were seen for pro-saccade and COWAT scores between the groups. On the cognitive assessments, patients with their dominant hand impaired (n=16) did not differ from those without (p's>0.05).

Conclusion: Preliminary results indicate assessment of EF using a short novel hands-free battery is feasible, during acute hospital rehabilitation. This research may support later studies on assessing the rehabilitation needs of manually-impaired adults.

T55: Control of Posture and Movement with Respect to Gravity by Setting the Referent Orientation of the Body

Aditi Mullick[1,3], Szu-Chen Hsu[2,3], Sandeep Subramanian[3,4], Nicolas Turpin[3,5], Anatol Feldman[3,4], Mindy Levin[1,3]

[1]School of Physical and Occupational Therapy, McGill University, Montreal, QC, Canada, [2]Neuroscience Program, McGill University, Montreal, QC, Canada, [3]Center for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR), Laval, QC, Canada, [4]Department of Neuroscience, Université de Montréal, Montreal, QC, Canada, [5]School of Rehabilitation, Université de Montréal, Montreal, QC, Canada

It has been suggested that multiple muscles of the body are controlled as a coherent unit based on the difference between the referent body configuration specified by the brain and the actual, body configuration. The referent configuration is the configuration at which muscles begin to be activated. We suggest that there are referent body configurations that are used to orient actual body postures (straight or leaned) during standing and most body movements in humans and animals relative to gravity. In other words, we suggest that neural control levels can specify a referent body orientation (R) at which multiple muscles of the body reach their activity minimum. Under the influence of gravity, the body is deflected from the referent direction to a direction Q, at which the emerging muscle activity results in forces that balance gravitational forces and body stability is maintained. This hypothesis predicts that during back-and-forth movements, R and Q may momentarily coincide, bringing the activity of multiple muscles of the body to a minimum. We tested this prediction by analyzing the activity of multiple body muscles during rhythmical changes in the body orientation during standing. To manipulate R and create situations in which minima occur, participants were required to stand on 3 surface orientations, ascending, horizontal, and descending, and perform whole body sways and mini squats. EMG minima were identified from EMG signals recorded in 11 muscles across the body and the body postures at which EMG minima occurred were determined. Global minima were identified in all conditions, both in swaying and squatting movements. The EMG minima occurred in 20%-82% of movements cycles. The postures at which global EMG minima occurred were different in different conditions. Preliminary results thus confirm the hypothesis. This study contributes to the understanding of how posture and movement are controlled in the gravitational field. It also extends the previous suggestion that multiple muscles of the body are controlled as a coherent unit depending on the difference between the actual and referent configurations of the body.

T56: Improving Motor Function After Stroke by Application of Electrical Theta-Burst Stimulation via Implanted Electrodes

Laura Boddington, Jason Gray, John Reynolds

Department of Anatomy, Brain Health Research Centre, University of Otago, Dunedin, Otago, New Zealand

Interhemispheric inhibition (IHI) may increase following stroke, which can negatively impact on recovery. In anaesthetized rats we have previously shown that application of low-intensity electrical stimulation in an intermittent theta-burst stimulation (iTBS) pattern to the motor cortex can abolish interhemispheric inhibition (IHI) onto the opposite hemisphere, which suggests it may be beneficial if applied therapeutically for stroke.

We have now shown that in the rat photothrombotic model, similar application of iTBS via an implanted electrode in the contralesional homologous motor cortex can improve functional recovery. In our study, one three-minute session of TBS or sham stimulation was applied twice weekly for three weeks commencing either 3, 10, or 31 days after stroke induction and recovery of forelimb function was assessed throughout using a grid walking test. A further group of rats received five three-minute sessions of TBS, each spaced by 10 minutes, five days a week for three weeks. After behavioural assessments, all rats were anaesthetized with urethane, and *in vivo* intracellular sharp electrode recordings were made in the peri-lesional motor cortex to measure IHI and excitability.

Application of intermittent TBS (iTBS) beginning 3 days after stroke improved forelimb function compared to both sham stimulation and continuous TBS (cTBS) (P<0.05; n=8 per group). Early implantation of electrodes after stroke and acute commencement of stimulation may not be desirable in the clinical setting. Therefore two further groups received stimulation starting at later time points. Commencing iTBS 10 days after stroke trended towards enhanced early recovery compared to cTBS and sham stimulation (n=6-8 per group). No differences were seen between groups (n= 7 per group) when stimulation began 31 days after stroke induction. However, preliminary data obtained by applying stimulation more intensively indicates that within-session repetitions of TBS can further enhance the effects on recovery, when stimulation is commenced 10 days following stroke induction.

These data show that applying infrequent contralesional electrical TBS early after stroke can enhance recovery but its effectiveness reduces with increasing delay in commencement. However, our preliminary data involving more intensive application of stimulation at more clinically translatable time points shows enhancement of recovery of motor function, consistent with enhanced effects on motor function by repeated applications of TBS applied using magnetic stimulation.

F1: Anxiety and Depression in Patients with Malformations of Cortical Development and Incomplete Hippocampal Inversion

Bhoopathy R M, Arthy B, Vignesh S S, Srinivasan A V

Madras Medical College, chennai, India

Background of the study: Anxiety and depression often lowers the quality of life. The frequency of occurrence of seizure, presence of structural abnormalities of the brain and antiepileptic medication has significant adverse effect in anxiety and depression of persons with intractable epilepsy. Hence we wanted to study the anxiety and depression levels in intractable seizures with Malformations of Cortical Development (MCD) and Incomplete Hippocampal Inversion (IHI) or malrotation of hippocampus.

Main Objective: 1) To find out the prevalence of anxiety and depression in patients with MCD and IHI.
2) To compare the anxiety and depression levels in patients with intractable epilepsy with structural abnormalities (MCD & IHI) and without structural abnormalities.

Methods: Three groups of patients with intractable epilepsy were considered for the present study from 410 patients attended our epilepsy clinic at Institute of Neurology, Madras Medical College. Group I - 41 patients with no abnormalities of brain, b) group II - 17 patients with MCD, c) group III – 30 patients with IHI. Groups were classified based on the 1.5 T MRI imaging with PSGR volumetric studies. Patients were then administered Multiphasic personality questionnaire who IQ scores above low average intelligence in weschlers adult intelligence scale.

Results: From the multiphasic personality questionnaire administered anxiety and depression score above cut off point were observed in 9 &12 patients in group I, 1 & 7 patients in group II and 10 & 11 patients in group III. It was also observed that all epilepsy patients had high prevalence of depression than anxiety. The mean score for anxiety and depression were 8.36 & 6.17 in group I, 6.82 & 6.41 in group II and 9.63 and 6.63 in group III patients. Independent samples kruskal –Wallis Test showed significant difference in anxiety scores across the group ($p<0.05$). No significant difference was observed for depression between the groups.

Conclusion: Anxiety and depression are highly prevalent in intractable seizure with normal MRI findings as well as in patients with MCD and IHI. Subjects in MCD group had low average intelligence compared to other two group thus they showed reduced prevalence of anxiety.

Conflict of interest: nil

F2: Increased Interhemispheric Coherence During Transcallosal Inhibition Assessment in Chronic Stroke: A Preliminary TMS-EEG Investigation

Michael Borich[1], Lewis Wheaton[2], Sonia Brodie[3], Bimal Lakhani[3], Lara Boyd[3]

[1]Emory University, Atlanta, Georgia, USA, [2]Georgia Institute of Technology, Atlanta, Georgia, USA, [3]University of British Columbia, Vancouver, British Columbia, Canada

Introduction: Reorganization and remodeling of motor network connections contributes to recovery of arm function after stroke. Changes in effective network connectivity in humans after stroke can be studied using concurrent transcranial magnetic stimulation (TMS)-electroencephalography (EEG). The primary objective of this study was to use imaginary coherence (IC) analysis of TMS-evoked EEG responses to directly characterize interhemispheric interactions between the primary motor cortices (M1s) in individuals with stroke.

Methods: Ten participants with chronic ischemic stroke in the right (n=5) or left (n=5) hemisphere and four age/gender matched healthy controls were tested. Standard TMS procedures were conducted bilaterally. Transcallosal inhibition (TCI) was evaluated by delivering single suprathreshold (150% resting motor threshold) TMS pulses over M1 while performing an ipsilateral grip force contraction (50% maximum). Suprathreshold TMS pulses were also delivered at rest. 64-channel EEG recordings were collected concurrently during TMS assessments.

All data pre-processing steps were performed in EEGLAB. Epochs were extracted for each participant and concatenated within each group for IC analysis. Post-TMS (0-300ms) IC values between electrodes overlying M1 (C3, C4) bilaterally were calculated within the beta frequency band (15-30Hz) as the primary dependent measure of interhemispheric IC. Secondary analyses subdivided the stroke group based on lesion hemisphere. Level of physical impairment was evaluated using the upper extremity portion of the Fugl-Meyer (FM) Assessment.

Results: Individuals with chronic stroke showed greater TMS-evoked interhemispheric IC compared to controls (p=.017) during TCI assessment. No differences were seen during the rest condition. Greater interhemispheric beta IC during TCI was observed in participants with lesions in the right hemisphere regardless of stimulation site. Participants with lesions in the left hemisphere exhibited greater arm impairment (median FM score: 16) compared to individuals with right hemispheric lesions (median FM score: 57).

Discussion: Preliminary findings suggest increased interhemispheric interactions between M1s during an active motor state are present in chronic stroke and may contribute to persisting disability.

F3: Effect of Resveratrol on Relapsing-Remitting Multiple Sclerosis

Matthew Davis[2], Pradeep Sahota[1,2] Mahesh Thakkar[1,2]

[1]Harry S. Truman Memorial Veterans Hospital, [2]University of Missouri School of Medicine, Columbia, MO, USA

The use of meta-analysis in basic biomedical research has increased in recent years due to differences in genetically modified mice producing inconsistent results. Resveratrol (RSV) is a naturally occurring polyphenol that has been shown to affect numerous biological pathways, leading to many health benefits. Several of these benefits include anti-inflammatory and neuroprotective properties that have implicated RSV as a possible therapy for relapsing remitting multiple sclerosis (RRMS). Recent research with RSV has been focused on a mouse model of MS called experimental autoimmune encephalomyelitis (EAE), but results have not been consistent. In the present study, we performed a meta-analysis of the data related to the effect of RSV on RRMS. The meta-analysis revealed a slight delay in the onset and progression of EAE in mice treated with resveratrol, as well as a decrease in peak symptom severity determined by a clinical scale score. Overall, mice treated with EAE showed a slower disease progression, including the number of days to reach peak clinical score and the number of days it took for the mice to reach minimum relapse score. This study suggests that, despite many positive effects, RSV has not shown statistically significant results as treatment for regulating the clinical presentation of EAE. Meta-analysis will be run on other aspects of the effect of RSV on RRMS before presentation, including its neuroprotective effect, quantified by level of retinal ganglion cell (RGC) axon damage and number of spinal cord lesions with preliminary analysis indicating a significant positive effect following treatment.

F4: The Effect of Antispasmodic Medications on Recovery During Inpatient Rehabilitation After Acute Traumatic Spinal Cord Injury

Eric R. Theriault[1,4], Vincent Huang[2], Gale Whiteneck[3], Marcel P. Dijkers[2], Noam Y. Harel[2,4]

[1]New York Institute of Technology, Old Westbury, NY, USA, [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA, [3]Craig Hospital, Englewood, CO, USA, [4]James J. Peters VA Medical Center, Bronx, NY, USA

Objective: Recovery from spinal cord injury (SCI) and other neurological disorders occurs partly through activity-dependent neural plasticity. By inhibiting neural activity, we hypothesize that antispasmodic medications may reduce plasticity and adversely affect outcomes after SCI. We queried the SCIRehab database to determine whether use of antispasmodic medications during inpatient rehabilitation affected neurological and functional outcomes during the first year after acute traumatic SCI.

Design: Retrospective analysis of prospectively obtained data.

Participants/methods: The SCIRehab study collected data on patients with traumatic SCI admitted to acute inpatient rehabilitation at six centers between 2007 and 2009. We analyzed the patient-level database for International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) grade and level; Functional Independence Measure (FIM); and types and doses of antispasmodic medications administered. Patients were considered to have received antispasmodic medications if they received at least 5 doses of muscle relaxants, benzodiazepines, or botulinum toxin during inpatient rehabilitation. Data was analyzed at inpatient admission, discharge, and one-year follow-up.

Results: 1,376 patients, 1111 male and 265 female, with an average age of 37.6 (range 12-88), were included in the analysis. 60.3%, 35.0%, and 4.7% were injured at the cervical, thoracic, and lumbosacral levels, respectively. 49.5% were ISNCSCI grade A, 16.5% were grade B, 18.5% were grade C, and 15.6% were grade D. Motor FIM score at admission averaged 23.5 (95% CI 22.9-24.0).

During acute inpatient rehabilitation, 686 patients (49.9%) received at least 5 doses of antispasmodic medications. Patients with cervical injuries were more likely to receive antispasmodic medications (58.1%) than those with thoracic (37.6%) or lumbosacral (35.4%) injuries.

After controlling for baseline injury severity and level at inpatient admission, motor FIM scores at inpatient discharge were significantly higher in patients not given antispasmodic medications (53.8, 95% CI 52.7-54.9) than in those who received antispasmodic medications (48.5, 95% CI 47.4-49.6) ($p<0.0005$). Likewise, motor FIM scores at one-year follow-up were significantly higher in patients not given antispasmodic medications: 63.9 (95% CI 62.3-65.5) versus 59.9 (95% CI 58.2-61.5) ($p=0.001$). These effects persisted after performing Rasch transformation - baseline-adjusted, Rasch-transformed FIM motor scores were higher in those not given antispasmodic medication: at discharge, 48.4 (95% CI 47.7-49.1) versus 45.4 (95% CI 44.7-46.2) ($p<0.0005$); at one year, 57.5 (95% CI 56.2-58.9) versus 55.3 (95% CI 53.9-56.6) ($p=0.022$). Antispasmodic medication did not significantly affect discharge ISNCSCI grade.

Conclusion: Antispasmodic medications may adversely affect functional recovery during inpatient rehabilitation from acute traumatic SCI. We speculate these consequences could be mediated by a combination of reduction in neural plasticity and other drug side effects. Randomized prospective studies are needed to further evaluate the effect of antispasmodic medication on neural and functional recovery.

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F5: Paired Stimulation to Increase Cortical Transmission to Hand Muscles

Lok Yung[1], Shivani Kastuar[2], Jason B. Carmel[3], Ann M. Spungen[1,2], William A. Bauman[1,2], Noam Y. Harel[1,2]

[1]James J. Peters VA Medical Center, Bronx, NY, USA, [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA, [3]Burke Medical Research Institute, White Plains, NY, USA

Objective: After neurological injury, repetitively activating spared circuits strengthens synaptic connections. We aim to use a novel combination of non-invasive magnetic and electrical stimulation to strengthen connections between motor cortex and hand muscles in subjects with cervical SCI or ALS.

Design: Prospective crossover device intervention pilot study (clinicaltrials.gov NCT02469675).

Participants/methods: Two groups of participants are being studied: individuals with chronic incomplete cervical SCI (n=12), and those with definite or probable ALS (n=6). After baseline testing, subjects undergo 7 combinations of unpaired or paired magnetic and electrical stimulation: transcranial magnetic stimulation (TMS) over the hand motor cortex, monophasic peripheral nerve stimulation over the median nerve at the wrist, or biphasic cervical root stimulation transcutaneously across the neck. Each session comprises unpaired or paired stimuli every 10 seconds for 20 minutes (120 stimuli). Paired stimulation is timed for TMS pulse arrival at cervical motor neurons either 1.5 ms before or 10 ms after electrical pulse arrival. Functional and physiological testing is conducted at baseline and 0, 15, 30, and 90 minutes post each intervention. Key outcome measures include grip strength dynamometry, timed performance on a hand dexterity test, amplitude of abductor pollicis brevis motor evoked potential, flexor carpi radialis H-reflex responses, and duration of the 'cortical silent period' after TMS stimulation during APB contraction.

Results: Preliminary results from the first subjects to undergo paired stimulation will be presented. We hypothesize that one session of paired stimulation augments corticospinal transmission for at least 30 minutes when electrical pulses are timed to arrive at cervical motor neurons 1.5 ms after TMS pulses. Cervical electrical stimulation is anticipated to demonstrate equal or superior efficacy to median nerve stimulation. We speculate that paired stimulation facilitates cortical transmission to hand muscles through spike timing-dependent plasticity.

Conclusion: The cervical stimulation technique offers several advantages over other approaches to neural stimulation: it is non-invasive, it activates multiple levels and both sides simultaneously, and it has the ability to target novel interaction sites for convergent peripheral and corticospinal input onto cervical motor neurons. These features offer the potential to strengthen cortical control over multiple arm and hand muscles using one stimulation paradigm.

Support: VA RR&D grants B0881-W and B9212-C.

F6: Threshold Position Resetting Suppressing both Stretch Reflexes and Background Muscle Activity in Response to Prolong Muscle Lengthening

Nicolas Turpin[1,3], Rim Rahal[1,3], Sandeep Subramanian[2,3], Mindy Levin[2,3], Anatol Feldman[1,3]

[1]Department of Neuroscience, Université de Montréal, Montréal, Canada, [2]School of Physical and Occupational Therapy, McGill University, Montréal, Canada, [3]Center for Interdisciplinary Research in Rehabilitation of Greater Montreal, Montréal, Canada

Since the work of Sherrington (1906), it has been recognized that, together with other proprioceptive reflexes, the stretch reflex (SR), i.e. position- and velocity-dependent resistance to muscle lengthening, plays a fundamental role in the control and stability of posture and movement. The spatial threshold of the SR, i.e. the muscle length or respective joint angle at which the SR begins to act is broadly regulated by spinal and supra-spinal systems in a task-specific way. We tested the hypothesis that the SR threshold can be reset to suppress both SR reactions and background muscle activity in response to high amplitude lengthening, thus preventing overstretching active sarcomeres. The forearm and hand of subjects (n=12) were placed on a horizontal manipulandum. Elbow flexor or extensor muscles were pre-activated by compensating an external load (1-3 Nm) applied to the manipulandum by a torque motor. The muscles were stretched by rotating the manipulandum by 60 ° at different velocities (8-120°/s) randomly selected for each trial. EMG signals (biceps brachii, brachioradialis, triceps brachii lateralis and medialis), displacement and velocity were recorded. In training trials and subsequent experimental trials, subjects were instructed to abstain from intentionally modifying their responses to perturbations. Trials in which subjects changed EMG levels prior to stretch onset were excluded. SR responses to muscle stretch (lengthening), if present, were minimal and occurred at latencies of 25-35 ms and after about 70 ms the EMG activity was suppressed for about 80 ms. After that the stretched muscles were reactivated during the ongoing muscle lengthening. Results are consistent with the notion of resetting of spatial thresholds for muscle activation, rather than with suppression (gating) of the SR in time. In general, threshold resetting is used not only to prevent muscle overstretching but also in the control of intentional movement. By doing so, the nervous system converts posture-stabilizing to movement-producing mechanisms, thus solving the classical posture-movement problem. Spatial threshold resetting can also be used to prevent falls in subjects standing on a platform that is suddenly tilted. The possible relationship between the notion of SR threshold resetting and the clasp-knife phenomenon in some neurological conditions is discussed.

F7: Track-Weighted Functional Connectivity in the Sensory Discrimination Network Correlates with Haptic Performance: A Preliminary Study in Stroke

Alexandra Borstad, Petra Schmalbrock, Deborah Nichols-Larsen

The Ohio State University, Columbus, OH, USA

Purpose/Hypothesis: Complex haptic tasks such as sensory discrimination require efficient processing between multiple brain areas. Novel methods, which combine the structural and functional imaging, such as track-weighted functional connectivity (TW-FC) proposed by Calamante and colleagues, may be sensitive to, and inform our understanding of the neural correlates of haptic performance. The purpose of this preliminary study was to 1) measure the test re-test reliability of TW-FC 2) to compare TW-FC in the sensory discrimination network in stroke and control participants. We hypothesized that 1) TW-FC would be reliable and sensitive to stroke-control group differences and 2) TW-FC would correlate with sensory discrimination performance.

Subjects: Ten community-dwelling individuals with hemiparesis as a result of chronic stroke, with mild to moderate deficits in upper extremity function and 10 age, gender and handedness neurotypical controls provided written consent to participate in this IRB approved study. The mean (SD) age was 67(10) years for post-stroke and 65(10) for controls. Chronicity of poststroke participants was 27(26) months.

Materials/Methods: Behavioral outcomes were monofilaments, the Hand Active Sensation Test (HASTe) and the 6-item Wolf. A 3 T MR scanner (Philips, Achieva, The Netherlands) with a body transmit and 8-channel receiver coil was used for structural and functional MRI scans. Blood oxygen level dependent (BOLD) T2* weighted functional MRIs in the transverse plane were obtained using Gradient Echo-Echo Planar Imaging with parallel imaging and a sensitivity encoding reduction factor of 2. (TR/TE=3000/35ms, flip angle=90°, FOV=230x230x140mm, matrix=80x80 interpolated to 128x128). Functional MRI data was analyzed using FSL. Diffusion tensor images were acquired in the axial plane with parameters: TR/TE=8000/68 ms, FOV=230x230x140mm, Matrix=116x114, Slice thickness/ gap=2.0/0.0mm, two b-values 0 and 1000 s/mm2, diffusion weighting gradient directions=60, SENSE reduction factor of 2, scan time of 9 minutes. TW-FC maps were generated using tools in MRtrix3.

Results: Between group differences were not statistically significant for either somatosensory measure. HASTe scores and TW-FC values were normally distributed. Paired t-tests revealed no between group differences for the 3 TW-FC ROI's examined: white matter, sensory discrimination network or the whole brain. TW-FC of the white matter was significantly related to age (r=0.62, p=0.003), lesion volume (r=0.65.p=0.044), chronicity (r=0.81,p=0.004), and right HASTe scores (r=0.65, p=0.002) but was not related to touch perception, 6-item Wolf, or brain volume. TW-FC was 1.9% different across ROI's described by Willats, 2014.

Discussion: This preliminary study suggests the TW-FC method, which fuses functional connectivity and structural brain information into a single quantifiable image, is sensitive to neural differences related to haptic performance. TW-FC may be superior to other connectivity methods for longitudinal analysis as the test-retest differences were low.

F8: Does Delayed Peroneal Activation in Response to a Sudden Underfoot Perturbation during Gait Predict Injurious Falls in the Elderly with Diabetic Peripheral Neuropathy?

Hogene Kim[3], Lara Allet[4], Trina DeMott[2], James. K. Richardson[2], James. A. Ashton-Miller[1]

[1]University of Michigan, Department of Mechanical Engineering, Ann Arbor, MI, USA, [2]University of Michigan Health System, Department of Physical Medicine & Rehabilitation, Ann Arbor, MI, USA, [3]National Rehabilitation Center, Seoul, Republic of Korea, [4]Hôpitaux Universitaires de Genève, Geneva, Switzerland

Background: Elderly with diabetic peripheral neuropathy (DPN) have a higher risk of falling and fall-related injuries, especially while walking on irregular surfaces. A slow nerve conduction velocity, common in patients with diabetes mellitus, may play a role. The delayed muscle feedback reaction time (fRT) in diabetes patients' lower extremities may lead to an ineffective reaction in response to an unexpected event. Therefore, the aim of this study was to investigate whether lower limb fRT during gait in response to a sudden underfoot perturbation predicts fall-related injuries in the elderly with DPN.

Methods: 41 elderly with and without DPN (20 female, mean 69.1 yrs) participated in this trial. All participants had a gait evaluation. They were equipped with a pair of custom sandals and were asked to walk 60 times at a comfortable speed on a 10 m level walkway. During each gait trial a discrete 16 mm-high medial (MP) or lateral (LP) underfoot perturbation might be suddenly presented once from the sandal sole under either foot and on any step. Overall the underfoot perturbations (total 8 MP and 8 LP with 4 on each side) were presented in 16 of the 60 trials. Simultaneously fRT measurements in frontal lower limb muscles of peroneus longus, medial soleus, and gluteus medius were made using wireless electromyography electrodes (EMG). The fRT in the recovery steps were compared with unperturbed fRT using post-hoc t-test ($p<0.01$). Participants were then followed for fall-related injuries over a year using self-report and diaries.

Results: Among 31 subjects with valid EMG data, 14 elderly (45.1% of total participants, 71.4% of elderly with DPN) reported a fall-related injury and 12 elderly (75% of normal subjects) had no falls during the following year. In response to a MP, peroneal activation in the elderly without a reported fall was significantly earlier for the first and second post-perturbation recovery steps (1st:-36.5(6.5)ms(p=0.008),2nd:-50.3(38.1) ms(p=0.016)) compared to unperturbed steps. However the peroneal activation in participants who reported a fall-related injury remain unchanged during the first recovery step but became significantly earlier during the second recovery step (1st:1.0(13.5) ms (p=0.116), 2nd:-31.9(4.5) ms (p=0.001)).

Discussion: These finding suggest that earlier peroneal fRT during the first post-perturbation recovery steps is associated with injurious falls in the elderly patients with DPN. Earlier peroneal fRT in the elderly who reported a fall-related injury were delayed during the second recovery step. The perturbing sandal may be a useful assessment to understand neuromuscular functioning in these patients. Future studies might examine the correlation between recovery step kinematics and lower limb fRT during gait.

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F9: Neural Correlates of Attentional Demands Associated with Dual-Task Walking

Samir Sangani[1], Taichi Kurayama[2], Joyce Fung[1,3]

[1]Jewish Rehabilitation Hospital, Feil/Oberfeld/CRIR Research Centre, Laval, Quebec, Canada, [2]Chiba University, Chiba, Japan, [3]McGill University, School of Physical and Occupational Therapy, Montreal, Quebec, Canada

Walking while simultaneously performing another task requires divided attention, e.g. holding a cup without spilling. Stability control during gait alone requires attention, which may be compromised as the cognitive demand increases. The impact of dual-tasking on biomechanical and neural components is yet to be explored. Our primary goal was to investigate gait pattern changes and the neural correlates of complex dual-task walking using functional near-infrared spectroscopy (fNIRS). Healthy young adults (n=11) and a stroke participant walked on a 3m long force-sensing treadmill (CMill, Motek-Forcelink). Cortical activation was acquired with a NIRScout system (NIRx) using a custom-built cap covering the frontal cortex. The protocol included repeated block trials consisting of four alternating blocks of standing (20s) and walking (25s) at a comfortable speed determined prior to the experiment. Five walking trials were performed, each consisting of four randomized conditions including holding a Styrofoam cup that was empty or filled with water, jelly or hot liquid. Participants held the cup in the dominant or non-paretic hand. Primary outcomes included stride length, step width, stride duration, center of pressure displacements and gait variability (% coefficient of variation in stride duration). The cortical hemodynamic response was quantified by concentration changes of oxygenated hemoglobin (oxyHb) in the frontal cortex. Cortical response maps were determined based on the general linear model using SPM (nirsLAB). Walking with a cup filled with hot liquid was associated with a slight decrease in step width and gait variability in all healthy participants but not the stroke individual. The decrease in step width suggests that all subjects adapted to the back-and-forth slosh frequency of the fluid by adjusting their gait so as to suppress the resonant slosh frequency thereby preventing any spillage. In healthy controls, walking while holding jelly was associated with activation of the supplementary motor area (SMA), whereas holding hot liquid resulted in activation of the premotor cortex (PMC) and dorsolateral prefrontal cortex (DLPFC), which are associated with selective attention. Cortical activation in the stroke participant demonstrated increased activation in the contralesional DLPFC and medial SMA while walking and holding either jelly or water. Absence of significant changes in biomechanical gait parameters suggests that during complex dual-task locomotion, the brain can allocate the required cortical resources to account for increased attentional demands without modifying the inherent locomotor pattern.

F10: Intensive Upper Limb Neurorehabilitation with Virtual Reality in Chronic Stroke: A Case Report

Odile Chevalley[1], Thomas Schmidlin[2], Daniel Perez-Marcos[3], Gangadhar Garipelli[3], Robert Leeb[2], Cyntia Duc[3], Ron Vollen[3], Philippe Vuadens[4], Tej Tadi[3], Olaf Blanke[1,2], José d.R. Millán[2,5]

[1]Laboratory of Cognitive Neuroscience, Brain-Mind Institute, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [2]Center for Neuroprosthetics, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [3]MindMaze SA, Ecublens, Switzerland, [4]Clinique Romande de Réadaptation, Sion, Switzerland, [5]Chair in Brain-Machine Interface, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Upper limb motor deficits are a frequent consequence of stroke, limiting patients in their daily life activities. The recovery process is slow and long, including several months or even years of rehabilitation, with the risk of diminishing patient motivation and involvement. Intensive therapy has been shown beneficial, improving the speed of recovery and the degree of independence. In this context, virtual reality (VR) based motor rehabilitation systems provide a potential complement to current therapy in order to intensify the therapy dose and to maintain patients motivation. This study was aimed at evaluating the rehabilitation dose and effect of a VR-based system (MindMotionPRO, MindMaze SA) that enables intensive training adapted to impaired upper limb motor skills in a game-like scenario. The interactive exercises engaged patient's shoulder, elbow and wrist movements with various levels of difficulty. The system provides real-time feedback of patient's performance, with an avatar reproducing his movements on the screen while performing different motor tasks (pointing, reaching, grasping).

A 50-year-old right-handed man, who had a left ischemic stroke 26 months earlier, was recruited for this study. He discontinued the conventional physiotherapy (once per week) in January 2015. At the time of recruitment (NIHSS=3), deficits in his right upper limb were notable in coordinating arm movements, with a Fugl-Meyer Assessment Upper Extremity (FMA-UE) score of 47/66 (Reflexes=4/4; Flexor synergy=9/12; Extensor synergy=5/6; Movement combining synergy=4/6; Movement out of synergy=5/6; Wrist=9/10; Hand=7/14; Coordination/Speed-Finger=4/6). One-hour sessions of intensive VR-based therapy were administered twice per week for five consecutive weeks (10 sessions in total) at the Clinique Romande de Réadaptation (Sion, Switzerland), starting on 21 April 2015. On average, the patient performed 804 goal-directed movements per session with his affected limb. Interestingly, the therapy dose continuously increased from 519 (session 1) to 809 (session 10) repetitions per day. In complement to the training, the patient engaged in daily sport activities. Post-treatment assessments showed an increase of 7 points in FMA-UE score (54/66), with improvements in proximal upper limb control and arm coordination (Flexor synergy=10/12; Extensor synergy=6/6; Movement combining synergy=6/6; Hand=9/14; Coordination/Speed-Finger=5/6). Moreover, the patient reported a positive experience with the technology and showed high levels of engagement during the sessions.

Based on this case report, we surmise that the use of the MindMotionPRO in clinical settings increases the feasibility of adjusting the rehabilitation dose upwards to speed up the recovery. The patient received one-hour intensive VR-based therapy twice a week in addition to sport activities, which contributed to an improvement in his motor outcomes. Intensive VR-based therapy brings thus promising perspectives for maximizing the efficacy of motor rehabilitation in stroke patients.

F11: Task-Oriented Arm Training in Standing Improves Both Anticipatory Postural Control and Upper Extremity Functional Outcomes in Stroke Patients

Sandy McCombe Waller, Chieh-ling Yang, Wan-wen Liao, Rogers Mark

University of Maryland Baltimore, Baltimore, MD, USA

Objective: Physical disability resulting from stroke is multifaceted, impacting both upper extremity (UE) and postural control, leaving patients at risk for immobility and falls. In current rehabilitation practice, training is often segmented and targets quite narrowly on one area of disability. As a result, carryover of isolated gains in physical abilities to meaningful context-specific functional performance is limited. To function in an upright world, training should prepare individuals to perform tasks in standing. Moving an arm to reach forward in standing involves anticipatory postural adjustments (APAs) of the legs that precede and accompany the goal directed arm movement, and reactive responses that stabilize balance and prevent falling. This integrated motor task requires the interaction of both corticospinal and subcortical systems. In previous work we identified delayed and reduced magnitude of APAs preceding a functional reach in standing using a cued reaching task using the neural probe of acoustic startle. We hypothesized training the arm in standing without explicit cues for postural adjustments would engage subcortical pathways that contribute to APAs while also improving UE function. We report in this presentation the changes in neural response to acoustic startle, effects on anticipatory postural control and UE functional outcomes after 6 weeks of arm training in standing. Subjects: Ten participants with stroke.

Methods: Neural response to acoustic startle was measured by the presence of startle induced movements during movement preparation and planning. Anticipatory postural control and reaching were evaluated with a cued reaching task in standing. APAs were characterized by onset and maximal displacement of the center of pressure (COP), and onset/offset of EMG from tibialis anterior, soleus. Paretic reach onset/offset and duration were measured. UE functional tests included the Fugl-Meyer UE Test (FM), Wolf Motor Function Test (WMFT), Box and Blocks and the University of Maryland Arm Questionnaire for Stroke (UMAQS). Training consisted of 6-weeks task oriented training with the paretic arm, in standing, with no explicit cues for postural weight shift.

Results: After training subjects demonstrated, an increase in startle induced movement responses, significant improvements in APAs as measured by onset and displacement of the COP. EMG timing improved post training to resemble timing characteristics of controls previously collected. Both the onset and timing of reaching improved significantly. UE functional gains were seen in FM scores and WMFT (time and weight). Gains in UMAQS scores indicated increased daily use of the arm after training.

Discussion/Conclusion: Results indicate gains in subcortical neural responses, anticipatory postural responses and paretic reaching in stroke as well as functional UE outcomes. Clinical Relevance: Arm training in the functional context of standing may better engage subcortical and corticospinal systems which can lead to gains in both postural control and function of the arm after stroke.

F13: Improvements in Visual Search Contribute to Visuomotor Learning

Christopher Perry[1], Tarkeshwar Sighn[1], Kayla Goins[1], Barbara Marebwa[2], Troy Herter[1]

[1]University of South Carolina, Columbia, SC, USA, [2]University of Trento, Trento, Italy

Introduction: Visual search is used to gather visual information by actively scanning the visual environment with eye movements (overt visual search) and peripheral vision (covert visual search). Previous studies have shown that visual search can improve with practice and expertise in motor skills is linked to efficient visual search. While these findings suggest that improvements in visual search may contribute to motor learning, previous research has not directly tested this hypothesis. Here we examine the extent to which improvements in visual search contribute to the acquisition of a novel visuomotor skill.

Methods: Eighteen young adults (20-31 years old) practiced a bimanual visuomotor task (Object Hit and Avoid Task) using an upper-limb robotic device (KINARM Endpoint Lab, BKIN Technologies, Kingston, Canada). In this task, objects (eight distinct geometric shapes) moved towards the subjects who used virtual paddles displayed on each hand to hit away two target shapes (Targets; n = 200), and avoid hitting the six distractor shapes (Distractors; n = 100). Each task trial lasted approximately two minutes, and the shape, location, and movement speed of individual objects was varied randomly to ensure every task repetition was distinct. Subjects completed six repetitions of the task once a week for six weeks. Object shapes assigned to Targets and Distractors varied weekly. Eye and hand movements were recorded to investigate the influence of visual search and limb-motor control on task performance.

Results: Task performance, as measured by Targets hit and Distractors avoided, increased across all six weeks. Task performance improved rapidly during the first week (acute phase) followed by slower improvements over the over 5 weeks (chronic phase). We observed that acute improvements were more coupled to the number of targets that were overtly viewed with smooth pursuit and the number of targets that were successfully hit following pursuit (overt success). Furthermore, chronic improvements appeared to be more linked to increases in success avoiding distractors and hitting targets that were viewed peripherally (covert success). Improvements in task performance did not appear to be coupled to changes in limb motor control. Conclusions: These results provide direct evidence that improvements in visual search can contribute to visuomotor learning. Our data also shows that both overt and covert visual search contribute to motor learning during acute and chronic phases, respectively.

F14: Comparing Three Dual-Task Methods and the Relationship to Physical and Cognitive Impairment in People With MS and Controls

Megan Kirkland, Elizabeth Wallack, Samantha Rancourt, Michelle Ploughman

Memorial University, St. John's, Canada

Background: Dual-tasking (combining a motor and cognitive task (DT)) is a potential measure to detect subtle impairments in people with multiple sclerosis (MS). The optimal DT method and the relationship between DT performance and disability is not clear.

Objective: We aimed to compare three DT test methods in MS subjects compared to controls and to determine whether cognitive (Montreal Cognitive Assessment (MOCA)) or physical disability (Expanded Disease Severity Scale; EDSS) was related to DT performance.

Methods: We recruited MS participants with low disability (<3 EDSS) and high disability (≥3 EDSS) and age (±3 years), gender and education (±3 years) matched controls. Participants walked at self-selected (SS) speed on an instrumented walkway (Protokinetics, Havertown, USA), followed by three DT walks in randomized order; DT ABC (reciting every second letter of the alphabet), DT 7 (serially subtracting 7's from 100) and DT 3 (counting upwards, leaving out multiples and numbers that include 3). Velocity, cadence, stride width, stride length, variability of stride length (coefficient of variation) and percentage time in double support data were collected. DT values were subtracted from SS values to determine the change in performance (DIFF) for each gait parameter.

Results: Of the three DT methods, DT 7 resulted in the most consistent changes in performance in 3 of 5 gait variables. MS groups (high disability (6 females, 3 males) and low disability (7 females, 4 males)) and controls (=13) reduced walking velocity and cadence and shortened step length during DT with no significant differences between groups. MS subjects exhibited altered adaptation compared to controls in percentage double support and stride width. MS subjects significantly increased percentage double support during DT compared to SS (High Disability: SS 35.14±9.78, DT 40.40±12.97; Low Disability: SS 28.61±2.80, DT 34.71±5.87; F=12.95, p<0.001) while controls did not (SS 27.25±2.57, DT 30.48±8.84). Control subjects widened stride width by about 1cm (DIFF -1.76±2.75; F=4.96, p<0.05) while MS subjects did not. In MS subjects, gait variables at SS speed were correlated with physical disability (measured using EDSS) but not cognition (MOCA score). However, the change in performance during DT was correlated with cognition rather than physical disability (percentage double support DIFF R=0.62, p=0.03). Change in performance during DT was not correlated with cognition in control subjects.

Conclusions: Our results suggest that of the three methods tested, DT 7 (counting backwards by 7s) produced the most consistent decrements in performance. Stride length, velocity and cadence do not change differentially in MS subjects compared to controls but stride width and percentage time in double support during DT is uniquely altered in MS subjects. Double support is likely an important indicator of DT impairment since it correlates with cognitive (but not physical) impairment.

F15: An Interprofessional Case Study: Training Health Profession Students in Clinical Exercise Therapy for People with Parkinson's Disease

Theresa Sweeny, Rebecca States, Amerigo Rossi

Long Island University (LIU), Brooklyn, NY, USA

Educational institutions that provide clinical training to health profession students are either mandated or strongly encouraged to provide interprofessional education (IPE) opportunities for students. Successful integration of appropriate faculty, students and community participants into sustainable interprofessional clinical training is challenging. This case study aims to describe a successful IPE model involving people with Parkinson's disease (PWP) that is currently operational at a major NYC university, and to identify the strengths and limitations of the model. Our IPE model is adapted from Hirsh's (2011) recommendations for community based health care for PWP. It requires integration of four elements: (1) committed faculty members from various health professions; (2) community participants with mild to moderate idiopathic PD who consistently participate in exercise; (3) a university gym area with dual action resistance machines and space for group cardiovascular exercise; and (4) health profession students from diverse disciplines who enroll in an elective 3-credit course entitled *Exercise Training in Individuals with Parkinson's Disease (ETIPD)*. The ETIPD course was offered in academic year 2014-15 and will continue in 2015-16. Twenty-four students from the Departments of Athletic Training, Health & Exercise Science (ATHES), and Respiratory Therapy have participated in the course which is growing in popularity. The faculty currently includes professors from Physical Therapy, ATHES and Nursing who complete a physical assessment of the PWP three times a year in an on-going prospective cohort research project on the effectiveness of consistent exercise in PWP. The faculty also supervises the bi-weekly exercise sessions. One faculty member (A.R.) has primary responsibility for the didactic lectures in the course with the other professors presenting selected didactic modules. One faculty member (R.S.) heads the research efforts. The nurse faculty member (T.S) has had specialized training in Parkinson's disease sponsored by the Parkinson's Disease Foundation Edmond J. Safra Visiting Nurse Faculty Program. The PWP were referred to the exercise program through a community Parkinson' s support group. All sessions are offered for free to individuals with PD with the backing of the investigators' university and the community support group. The current cohort numbers 27 PWP who consistently exercise two times a week for 10 weeks a semester during the academic year. The strengths of the model include the attachment of the exercise sessions to a university sponsored course, the collegial and friendly atmosphere of the exercise sessions, the strong support of the university and the community Parkinson's group, and, perhaps most importantly, the strong conviction of all involved that consistent exercise slows the progression of Parkinson's disease and helps the participants maintain self sufficiency. The major limitation of the model is the challenge of presenting the full 20-session the summer module when the exercise sessions are not part of the ETIPD course.

F16: Evidence for Interhemispheric Reorganization in Sensory Cortex Following Unilateral Upper Extremity Amputation in Humans

Benjamin Philip[1,2], Scott Frey[1,2]

[1]Washington University, St. Louis, MO, USA, [2]University of Missouri, Columbia, MO, USA

Deafferenting injuries (e.g. limb amputation) lead to reorganization of the somatosensory cortex, but the functional relevance of these changes remains unknown. Classic work in primate somatosensory cortex (S1) identified immediate and precise reorganizational changes in S1 ipsilateral to deafferentation, following reorganization in contralateral S1 after small deafferenting injuries (Calford and Tweedale 1990). Furthermore, following unilateral rat forepaw deafferentiation, stimulation of the radial nerve from the intact side is associated with bilateral increases in the blood oxygen-level dependent (BOLD) response in S1, which appears to reflect disruptions in interhemispheric functional connectivity (Pawela et al. 2010). Human unilateral amputees exhibit bilateral increases in cortical sensorimotor hand areas during use of the intact limb (Bogdanov et al. 2012), but it remains unknown whether such effects depend on reductions in interhemispheric inhibition between motor and/or sensory regions.

In an effort to determine whether similar effects occur in human S1, we developed an fMRI-compatible system to deliver cutaneous stimulation to the fingers of the intact hand, as well as the left or right sides of the lower face, of 15 unilateral traumatic amputees and 28 healthy adults matched for age, gender, and handedness. Amputees showed greater activity than controls in left (ipsilateral to stimulation) S1 during stimulation of the intact left hand. Activity in the former hand territory showed no between-groups difference in response to facial stimulation, nor any statistically significant correlations with phantom limb pain or time since amputation. To our knowledge, this is the first demonstration of interhemispheric transfer of plasticity in human primary somatosensory cortex. This phenomenon may allow physicians to influence deafferented cortex (e.g. contralateral to a hand with nerve injury) by therapies targeting the intact hand or cortex, thereby opening new avenues toward rehabilitation of patients with unilateral upper limb disability.

F17: Manual Asymmetry During a Bilateral Reach and Hold Task

Elizabeth J. Woytowicz[1], Jill Whitall[1,2], Kelly Westlake[1], Robert L. Sainburg[3,4]

[1]University of Maryland School of Medicine, Baltimore, MD, USA, [2]University of Southampton, Southampton, England, UK, [3]Penn State Milton S. Hershey Medical Center and College of Medicine, Hershey, Pennsylvania, USA, [4]Penn State University, University Park, Pennsylvania, USA

We have previously characterized interlimb and interhemispheric asymmetries for unilateral coordination tasks. This work has led to a model of motor lateralization in which one hemisphere is specialized for impedance control that is robust to unstable environmental conditions, while the other hemisphere is specialized for predictive mechanisms that can specify efficient and smooth trajectories under stable environmental conditions. We hypothesize that these two specializations are distributed across the arms during everyday bilateral tasks that involve holding and manipulating, such as when holding a baguette with one hand to slice it with the other hand. We predict that each hand should demonstrate different specializations for each of these task elements during bilateral behaviors. In order to test this hypothesis, we designed an experimental equivalent of the hold and slice task. In this task, performed in a virtual environment with the unseen arms supported by frictionless air-sleds, the arms are connected by a spring, while one hand maintains its position at the origin of the task, and the other moves to a series of targets distributed across a range of directions. Thereby, the reaching hand is required to take account of the spring load to make smooth and accurate trajectories, while the stabilizer hand must impede the spring load to keep a constant position. Right-handed subjects performed each of two sessions of this task, with the order of the sessions counterbalanced between groups. In one session, the right hand reached while the left hand stabilized, and the second session the left hand reached while the right hand stabilized. Our very preliminary results indicate a hand by task component interaction, such that the right hand showed better reaching performance, with faster and smoother (Jerk) reaching. In contrast, the left hand stabilized better, showing less displacement than the right hand. These findings suggest that the specializations of each cerebral hemisphere for impedance and predictive mechanisms are expressed during bilateral interactive tasks, such as the reach and hold task. To date, this is the first demonstration of the dynamic dominance hypothesis within the context of an asymmetric bilateral task. Further, once evaluated in non-disabled adults, future investigations within patients post-stroke could provide knowledge for the development of novel functional bilateral rehabilitation approaches.

F18: Modulating Transcallosal and Intrahemispheric Brain Connectivity with Transcranial Direct Current Stimulation (tDCS)

Xin Zheng, Gottfried Schlaug

Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

Background/Objective: Transcranial direct current stimulation (tDCS) can enhance or diminish cortical activity depending on the polarity of the stimulation. The inter-hemispheric disinhibition model after a stroke has been used to support the use of non-invasive brain-stimulation in stroke-lesioned brains, where decreased activity in one hemisphere can lead to uninhibited increased activity in the contralateral hemisphere which might interfere with the recovery process. This model has been developed mainly for the hand-motor system, where the effects of tDCS or transcranial magnetic stimulation on motor-evoked potentials (MEPs) and intra- and inter-hemispheric excitatory and inhibitory effects can be examined. Findings in the language/speech-motor system are less clear showing that both anodal and cathodal stimulation on either hemisphere can produce beneficial effects on language/speech-motor recovery. We aimed to examine physiological evidence of the inter-hemispheric disinhibition model in the language system through changes in inter- and intra-hemispheric connectivity due to tDCS.

Methods: Using an MR-compatible DC-Stimulator, we applied anodal stimulation to the right inferior frontal gyrus (IFG) regions of nine healthy adults while undergoing non-invasive cerebral blood flow imaging with arterial-spin labeling (ASL) MR imaging. Twenty additional subjects who underwent ASL-MRI without tDCS were used as a control group. The stimulation group underwent scanning for 26 minutes: the first 10 minutes were without stimulation (baseline), the next 8 minutes had the stimulation turned on (stim), and the final 10 minutes were without stimulation again (post-stimulation). All ASL images were then normalized and timecourses were extracted in regions of interest (ROIs), which were the left and right IFG regions, and the right supramarginal gyrus (SMG). Inter-hemispheric connectivity is taken as the correlation between left and right IFG and intra-hemispheric connectivity is taken as the correlation between right IFG and right SMG.

Results: The right, stimulated IFG timecourse showed a 10% increase in blood flow between baseline and the maximum of the stimulation phase, followed by a decrease in the post stimulation phase, where the average blood flow is still 3% higher than the baseline average. This elevated blood flow between post-stimulation and baseline is not seen in the other ROIs. Inter-hemispheric connectivity decreased significantly ($p<0.05$; r-scores from 0.67 to 0.53) between baseline and post-stimulation, while the intra-hemispheric connectivity increased significantly ($p<0.05$; r-scores from 0.74 to 0.81). The correlation scores did not change significantly in the control group over similar time intervals.

Conclusions: We showed that an MR-compatible DC stimulator and ASL-MRI can detect modulation of brain activity locally as well as in remotely connected brain regions. A decrease in inter-hemispheric connectivity with anodal stimulation, in conjunction with an increase in intra-hemispheric connectivity, suggests a more complex hemispheric interaction outside the motor system that might have to be taken into consideration when optimal stimulation paradigms are designed.

F19: Right Hemisphere Structures Predict Post-Stroke Speech Fluency

Ethan Pani, Xin Zheng, Andrea Norton, Jasmine Wang, Gottfried Schlaug

Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, USA

Objective: We sought to determine the contribution of (1) the right-hemisphere's speech-relevant white matter regions and (2) inter-hemispheric connectivity through the corpus callosum to speech fluency in the chronic phase of left-hemisphere stroke with aphasia.

Methods: We used fractional anisotropy (FA) to examine white matter underlying the right middle temporal gyrus (MTG), precentral gyrus (PCG), and pars opercularis of the inferior frontal gyrus (opIFG) as well as the corpus callosum (CC) and selected sub-regions thereof. We correlated FA values of these right-hemisphere and CC regions with speech fluency and efficiency measures and compared FA values of regions that significantly predicted speech measures with FA values of the same regions in healthy age-matched controls.

Results: FA values for the right MTG, PCG, and opIFG significantly predicted and were positively correlated with speech fluency. A multiple regression showed that the combination of right-hemisphere FA and left arcuate fasciculus lesion load (AF-LL), a previously identified biomarker of post-stroke speech fluency, improved our model for predicting speech fluency compared to AF-LL alone. FA of CC fibers connecting left and right supplementary motor areas (CC-SMA) was also correlated with speech fluency. FA of the right opIFG and PCG was significantly higher in patients than in controls, while FA of a whole CC ROI and the CC-SMA sub-region was significantly lower in patients.

Conclusions: Given the increase in FA observed in the right speech-motor homotops of patients relative to controls as well as the positive correlation between FA of the same regions and patient speech fluency outcomes, we hypothesize that compensatory, beneficial white matter reorganization occurred in the right hemisphere in patients. Lower FA values in the patient group CC ROIs are likely due to Wallerian degeneration and may have further contributed to right hemisphere changes.

F20: Effectiveness of Modified Constraint Induced Movement Therapy in a Group Setting as Compared to Individual on the Quality and Quantity of Upper Extremity Movement Recovery After Stroke

Rodrigo Rivas[1,2], Arlette Doussoulin[3], José Luis Saiz[4], Sarah Blanton[5]

[1]*Universidad de La Frontera, Departamento de Especialidades Médicas, Temuco, Chile,* [2]*Clínica Alemana Temuco, Servicio de Medicina Física y Rehabilitación, Temuco, Chile,* [3]*Universidad de La Frontera, Departamento de Pediatría y Cirugía Infantil, Temuco, Chile,* [4]*Universidad de La Frontera, Departamento de Psicología, Temuco, Chile,* [5]*Rehabilitation Center, Emory University, Atlanta, USA*

Background: Constraint-Induced Movement Therapy (CIMT) is a therapeutic strategy that has been show to improve the function of the upper limb affected by stroke. Although an extensive body of literature supports the positive impact of CIMT on neuroplasticity and the recovery of function, most research has evaluated an individual mode of delivery. However, evidence is limited for the application of CIMT protocol in a group setting.

Objective: To determine the effectiveness of a modified version of CIMT in a group setting as compared to individual, one-on-one basis on the quantity and quality of movement of the paretic upper limb.

Methods: Forty seven participants were analyzed and 36 patients were included. They were randomized into either a group or individual application of CIMT. The hemiparetic upper extremity quantity and quality of movement was evaluated using the self-reported, Motor Activity Log and each participant's clinical record at baseline, pre-treatment and post-treatment. *Inclusion Criteria*: Aged between 18 and 80 years, a single event of stroke confirmed by brain CT, with further evolution to 6 months the ability to sit independently, NIH Stroke Scale: 5 - 14 points, <2 points in the modified Ashworth scale, <4 points on the VAS, ability to perform a functional test of 20° of wrist extension and 10° in the extension of the fingers. *Exclusion Criteria*: Patients who may compromise sensory (visual-auditory), orthopedic limitations (use of cane), severe aphasia, failure to complete the inclusion criteria. The data were analyzed through an analysis of variance with a mixed factorial design 2x2. All patients signed informed consent.

Results: The median age 52.7±6.1 years, male were 66.7%, ischemic stroke were 63.9%, time since stroke 576±237 days. VAS: 1.55±1.18, modified Ashworth scale: 1.02±0.57. The median quantity and quality of movements (MAL) were in group pre-treatment (median): 1.79 and post-treatment (median): 3.09 and individual pre-treatment (median) 1.51, and post-treatment (median): 2.69. Subsequent to evaluate the groups after the intervention, it is important to note that while both methods improved the quantity and quality of movement, significant differences in favor of group mode with a value of $p = 0.04$.

Conclusion: This clinical trial provides evidence supporting the application of CIMT delivered in a group mode for 3 hours, to improve the performance of the paretic upper limb in daily activities. However the evidence is still limited in relation to this mode CIMT version.

Key words: Rehabilitation- Stroke-Upper Extremity

F21: Is Structural Connectivity of Basal Ganglia Associated with Learned Non-Use in Chronic Stroke?

Bokkyu Kim[1], Youngmin Oh[1,2], Richard Leahy[3,4], Justin Haldar[3,4], Nicolas Schweighofer[1,2], Carolee Winstein[1]

[1]Division of Biokinesiology and Physical Therapy at University of Southern California, Los Angeles, CA, USA, [2]Neuroscience Graduate Program at University of Southern California, Los Angeles, CA, USA, [3]Ming Hsieh Department of Electrical Engineering at University of Southern California, Los Angeles, CA, USA, [4]Brain and Creativity Institute at University of Southern California, Los Angeles, CA, USA

In those with mild to moderate stroke impairment, there can be a discrepancy between movement capability and daily use of the affected arm and hand. This is captured by the phrase, "he can, but does he?" This phenomenon may be a consequence of negative reinforcement resulting from affected arm use and positive reinforcement for less-affected arm use. The basal ganglia (BG), especially ventral striatum, are considered the neural reward center for reinforcement learning. Thus, the BG may have an important role in mediating the learned non-use phenomenon in chronic stroke. The primary aim is to investigate whether the structural connectivity of BG to other sensorimotor brain areas is associated with affected arm use. This study is part of a larger longitudinal Phase-I clinical trial of rehabilitation in chronic stroke (ClinicalTrials.gov ID: NCT 01749358). Individuals with mild to moderate motor impairment after stroke participated (N=24, average chronicity= 3.04 years). Structural brain images (T1-weighted MRI and DTI) were acquired, and processed using BrainSuite14a (http://brainsuite.org/). A total of twenty-four cortical or subcortical sensorimotor areas (Twelve regions of interests [ROIs] in each hemisphere) and a cerebellum ROI were chosen to construct a structural network. We calculated the Fractional anisotropy (FA) of each tractography between each ROI pair. A 25 X 25 FA matrix was generated to produce an undirected weighted graph. A weighted communicability graph was also computed from the raw FA matrix. Network metrics, including strength and degree, were calculated from FA and communicability graphs for each ROI. We calculated an asymmetric index (AI) of each network metric between an ROI and its homologous ROI in the other hemisphere. Motor Activity Log (MAL) was used to quantify the paretic arm use in daily activities. Linear regression analyses were used to test the relationship between connectivity metrics and MAL score. Significance level was set using Bonferroni correction for multipe comparisons (alpha=0.05/12=0.00417). There was no significant linear relationship between any network metrics and MAL score. However, the communicability strength AI (CSAI) of caudate nucleus showed the highest effect size on the MAL score among twelve CSAIs. 17% of variance in MAL score was explained by the caudate CSAI (p=0.024, Effect size [Cohen's f^2] = 0.21). Other ROIs' CSAI had smaller effect size than caudate CSAI on the MAL score (Cohen's $f^2 < 0.10$). This result provides partial support for our hypothesis that structural connectivity of BG is associated with affected arm use in chronic stroke. People with a higher caudate CSAI demonstrated less use of the affected arm in daily activities than those with a lower caudate CSAI. Future work should test whether a reduced structural connectivity of ipsilesional caudate nuclei is predictive of learned non-use, or is simply the result of affected arm non-use.

F22: Toward a Self-Calibrating Brain-Computer Interface for People with Tetraplegia

Beata Jarosiewicz[1,2], Anish Sarma[1,2], John Simeral[2,1], Daniel Bacher[1], Jad Saab[1], Brittany Sorice[3], Christine Blabe[4], Sydney Cash[3,5], Emad Eskandar[3], Krishna Shenoy[4], Jaimie Henderson[4], Leigh Hochberg[2,1]

[1]Brown University, Providence, RI, USA, [2]Dept. of VA Medical Center, Providence, RI, USA, [3]Massachusetts General Hospital, Boston, MA, USA, [4]Stanford University, Stanford, CA, USA, [5]Harvard Medical School, Boston, MA, USA

Brain-computer interfaces (BCIs) aim to restore communication and independence to people with severe motor disabilities by translating decoded neural activity directly into control of a computer cursor. However, nonstationarities in recorded brain activity can degrade the quality of neural decoding over time. Periodically interrupting ongoing use of the BCI to perform decoder recalibration tasks is time-consuming and impractical. In the ongoing pilot clinical trial of the investigational BrainGate2 Neural Interface System, we previously showed that typing performance in a self-paced, neurally controlled point-and-click communication interface can be maintained for hours, despite underlying signal nonstationarities, without requiring the user to pause to perform disruptive calibration tasks. This was accomplished using 3 innovations that address different aspects of neural signal nonstationarities: feature mean and variance tracking, decoder output bias correction, and retrospective target inference-based (RTI) decoder calibration, which uses data acquired during practical, ongoing BCI use to recalibrate the decoder. The current study extends self-calibration of the BCI to multiple days. On day 1, a BrainGate participant diagnosed with amyotrophic lateral sclerosis (ALS) (participant T6) performed the standard "center-out" decoder calibration task with presented targets, and then proceeded to self-paced typing. Then, on days 3, 5, 14, 35, and 42, with the aid of feature tracking and bias correction, the participant was able to proceed directly into self-paced typing using the previous session's last directional and click decoders. The decoders were updated periodically over the course of the day using RTI decoder calibration, without ever requiring the participant to perform explicit calibration tasks again after day 1. By eliminating the need for the user to perform daily calibration tasks with prescribed targets, despite nonstationarities in the underlying neural signals, this approach advances the potential clinical utility of intracortical BCIs for individuals with severe motor disability.

F23: Imperceptible Random Vibration Applied to Wrist Skin Increased EEG Evoked Potential for Fingertip Touch

Na Jin Seo[1], Kishor Lakshminarayanan[2], Brian Schmit[3]

[1]Medical University of South Carolina, Charleston SC, USA, [2]University of Wisconsin-Milwaukee, Milwaukee WI, USA, [3]Marquette University, Milwaukee WI, USA

The objective of this study was to investigate if cortical activity for sensing touch stimuli on the fingertip is affected by imperceptible white-noise vibration applied to wrist skin. Recent studies have demonstrated that fingertip tactile sensory thresholds improved with continuous, imperceptible, white-noise vibration applied to different locations in the upper extremity such as wrist, forearm, dorsum of the hand, or base of the palm in healthy adults as well as chronic stroke survivors. As such, vibration can be used to manipulate sensory feedback and improve dexterity, particularly during neurological rehabilitation. Nonetheless, the neurological bases for remote vibration enhanced sensory feedback are yet poorly understood. This study examined how imperceptible random vibration applied to the wrist changes cortical activity for fingertip sensation in healthy adults using electroencephalogram (EEG). We employed somatosensory evoked potential to assess peak-to-peak evoked response to light touch of the index fingertip with applied wrist vibration versus without. The peak-to-peak somatosensory evoked potential in response to fingertip touch significantly increased ($p < .05$). In addition, increased neural recruitment of the somatosensory, motor, and premotor cortex with wrist vibration was observed, corroborating an enhanced cortical-level sensory response motivated by vibration. It is possible that the cortical modulation observed here is the result of the establishment of transient networks for improved perception. This study results support the modulation of cortical-level of somatosensory processing using remote imperceptible vibration, providing the neurobiological basis for its further use in rehabilitation.

F24: From Noise to Music: Using Bayesian Statistical Parameter Estimation to Model Intra-Individual MEP Variability Before and After TBS for More Dynamic Biomarkers of Plasticity

Rachel Wurzman[1], Denise Harvey[1,3], Olufunsho Faseyitan[1,2], Daniela Sacchetti[1,2], Roy Hamilton[1,2]

[1]Laboratory for Cognition and Neural Stimulation, University of Pennsylvania, Philadelphia, PA, USA, [2]Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, [3]Moss Rehabilitation Research Institute, Elkins Park, PA, USA

Continuous theta burst stimulation (cTBS), an inhibitory subtype of repetitive transcranial magnetic stimulation (rTMS), is thought to induce plasticity in the stimulated cortical region and thus is frequently investigated as a treatment for neural injury. Cortical excitability and neuroplastic changes therein are measured by assessing increases or decreases in the mean amplitude of motor evoked potential (MEPs), the motor response to TMS. However, the therapeutic utility of rTMS (including cTBS) has been curtailed by a high degree of variability in responses to repetitive stimulation, even among healthy individuals.[1] Despite advances in understanding several factors contributing to inter-individual variability in the rTMS response, much less is known about the variability of MEP amplitudes within individuals, which may itself constitute a dynamic factor affecting the induction of plasticity. A more precise characterization of the intrinsic variability of MEP amplitudes during collection may add a valuable new dimension to hierarchical models predicting individual neuroplasticity responses to rTMS.[2]

This study used Bayesian Data Analysis (BDA) methods to explore the possibility that the induction of plasticity may be accompanied by changes in the shape of the distribution of sampled MEPs within a block, independently of changes to mean MEP amplitude. To enable simultaneous estimation of multiple descriptive parameters for sets of collected MEPs besides the mean (i.e., mode, spread, normality, and skewness), we employed Bayesian statistics to estimate parameter values and examine changes in the distributions of sampled MEPs peak-to-peak amplitudes collected before versus after cTBS. 30-35 MEPs were obtained from the right dorsal interosseous muscle of 31 healthy individuals using single-pulse, aperiodic TMS to motor cortex (M1). TMS pulse-strength levels were individually determined as the ratio of percent machine output required to elicit 1mV MEP amplitudes to resting motor threshold (rMT), and remained constant throughout the experiment. After baseline MEP collection, cTBS was administered for 40s (50-Hz triplets delivered at 5-Hz; 80% active motor threshold), followed by post-stimulation MEP blocks sampled at 0-min, 20-min, and 30-min.

Our results suggest that shape of the distribution of MEP amplitudes might be a dynamic variable in itself. For example, MEP amplitudes were not normally distributed and at baseline, and shape parameters (spread, normality, skewness) varied as a function of TMS pulse-strength, but not the mode. Following cTBS, TMS pulse-strength no longer predicts distribution shape parameters, which instead appeared to vary as a function of the mode MEP amplitude in a subset of subjects. Importantly, BDA does not assume that the data are normally distributed a priori. Rather, it precisely estimates central tendency and shape parameters without discarding "outlier" values, which are often eliminated for statistical expediency despite being potentially meaningful datapoints.[3] Accordingly, BDA outputs more faithful representations of intra-individual MEP variability for integration into inter-individual variability predictions.

F25: Paired Brain and Spinal Cord Stimulation to Strengthen Corticospinal Responses

Asht Mishra[1], Disha Gupta[1], Ajay Pal[1], Jason Carmel[1,2]

[1]Burke Medical Research Institute, White Plains, NY, USA, [2]Weill Cornell Medical College, New York, NY, USA

Spinal epidural stimulation has emerged as a powerful tool to raise the excitability of spinal cord circuits and to strengthen voluntary movement after injury. We sought to augment excitability of the corticospinal motor tract by pairing stimulation of its origin in motor cortex with stimulation of its end in the cervical spinal cord. All of the experiments were conducted in intact, anesthetized adult rats. We measured excitability of the motor system by electrically stimulating motor cortex and recording EMG in the contralateral biceps muscle. We created response curves by stimulating cortex at increasing intensity and compared curve under different conditions. We delivered epidural stimulation on the dorsum of the cervical spinal cord. We conducted 3 experiments. In the first experiment, we measured the effects of tonic 40Hz spinal epidural stimulation on EMG responses. We hypothesized that, like lumber epidural stimulation, tonic cervical spinal cord stimulation would augment EMG responses in a manner dependent on the intensity, polarity, and stimulation location. Indeed, tonic stimulation directed at the cervical enlargement produced robust augmentation of EMG with both cathodal and biphasic stimulation that increased with intensity. In the second experiment, we hypothesized that a single pulse of spinal epidural stimulation at discrete intervals after cortex stimulation would augment EMG responses. Latency was a crucial determinant, with 11ms being optimal. This timing coincides with the timing of the spinal cord dorsum potential recorded in the cervical cord after motor cortex stimulation, suggesting synergistic effects of corticospinal and large diameter sensory afferent stimulation. Finally, we asked whether repeatedly pairing of cortex and spinal cord stimulation at the optimal latency would induce learning in the spinal cord. We created a baseline response curve and also measured the spinal stimulation necessary to provoke EMG responses. We then delivered motor cortex stimulation followed 11 ms later by a single biphasic spinal cord pulse and repeated this every 2 seconds for 5 minutes for a total of 150 paired stimuli. We recorded a response curve and spinal thresholds immediately after the pairings and every 10 minutes thereafter. Paired stimulation caused a dramatic (>100%) increase in motor responses and the spinal threshold also decreased. Thus, we demonstrate plasticity in the intact corticospinal motor tract by repetitive pairing of brain and spinal cord stimulation that occurs at the level of spinal cord.

F26: Impaired Multi-Finger Synergies in Individuals with Multiple Sclerosis

Daniela Mattos[1,3], Hang Jin Jo[1], Elisabeth Lucassen[1,2], Mark L. Latash[1]

[1]Pennsylvania State University, State College, PA, USA, [2]Pennsylvania State University-Milton S. Hershey Medical Center, Hershey, PA, USA, [3]University of Delaware, Newark, DE, USA

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system that can result in impaired hand function. An important component of everyday hand actions is to ensure controlled stability of the combined action by a set of digits. We investigated multi-finger synergies stabilizing total force during a pressing task in twelve participants with mild and moderate MS and 12 age- and gender-matched control subjects. All subjects were tested during performance with their dominant and non-dominant hands. The subjects produced an accurate constant force level by pressing with four fingers on individual force sensors followed by a self-paced force pulse into a target. Finger inter-dependence (enslaving, E) was quantified using ramp force tasks performed by each finger. The uncontrolled manifold approach was used to compute a multi-finger synergy index during steady state and changes in this index (anticipatory synergy adjustments, ASA) in preparation to the force pulse. The MS group showed significantly lower maximal finger forces for both hands and higher enslaving among fingers when the lateral fingers (index and little fingers) were the task fingers. The MS group was also slower as compared to controls in the time to force peak. MS subjects showed significantly lower synergy indices than the controls during the steady-state phase and also demonstrated smaller and delayed ASA in preparation to the force pulse. These findings indicate that MS affects several aspects of multi-finger coordination including lower finger individuation, weaker force-stabilizing synergies, and decreased anticipatory adjustments in preparation to a quick action. These changes could be related to the impaired hand function observed in this population. Given that similar synergy changes are observed in patients with Parkinson's disease and multi-system atrophy, additional analysis is needed to explore possible differences in the indices of synergy in MS subjects with involvement of different pathways within the central nervous system.

F27: Training a Complex Arm Skill Transfers to Improved Simple Reaching Tasks and Modulates Corticospinal Excitability in Patients With Stroke

Nazaneen Zahedi, Robert McGrath, Shailesh Kantak

Moss Rehabilitation Research Institute, Elkins Park, PA, USA

Motor skill training involves acquiring novel movement capabilities through practice that leads to an improvement in the speed-accuracy tradeoff function, akin to acquiring real-world skills. Recent evidence indicates that skill learning is behaviorally and neuroanatomically distinct from motor adaptation and sequence learning. In this study we investigated the practice effects of a complex arm motor skill on change in speed-accuracy tradeoff (learning) as well transfer to a simpler functional reaching task. In a subset of patients, we explored the neural mechanisms of skill learning using transcranial magnetic stimulation (TMS). Specifically, we assessed the pre-post change in TMS-evoked recruitment curve and transcortical inhibition targeting the paretic triceps brachii. Participants with moderate stroke (n=10) practiced a complex motor task the goal of which was to navigate a cursor with their paretic arm through a virtual track as fast as possible without crossing the borders of the track. Performance changes during practice were characterized by improvements in accuracy while practicing within the prescribed movement time ranges. Learning was indexed by changes in the speed-accuracy tradeoff function measured at baseline, a day and approximately a month after practice ended. To assess the transfer to a non-practiced task, we examined the pre-post changes in goal-directed reaching to three different targets placed in front of the patient. All patients improved their performance on the practiced task. Following practice, there were improvements in the speed-accuracy tradeoff function that were retained over a month. Importantly, there was a significant improvement in the performance and control of non-practiced functional reaching task as evidenced by reduced movement times, higher peak velocities and shorter time-to-peak velocities after practice. Improved motor control was also reflected in improved efficiency indicated by decrease in the number of submovements during execution of the practiced as well as the non-practiced task. Neurophysiological data indicated an increase in the corticospinal excitability and decrease in transcallosal inhibition with training. Patients with stroke demonstrate improved performance and control of the trained paretic arm following practice of a complex arm motor task. This improved performance is accompanied by changes in the corticospinal and interhemispheric mechanisms. The most novel finding of our study is that learning of the complex task transfers to improved performance on an untrained simpler task. These findings have significant clinical implications suggesting that complex task practice may be helpful in driving performance and control improvements for simple tasks, particularly if the two (complex and simple tasks) share similar control processes. Corticospinal and interhemispheric changes likely underlie the efficient motor performance.

F28: Effects of Metformin and Enriched Rehabilitation on Recovery Following Neonatal Hypoxia-Ischemia

Sabina Antonescu[1,3], Matthew Jeffers[1,3], Jessica Livingston-Thomas[1,3], Cindi Morshead[2], Dale Corbett[1,3]

[1]University of Ottawa, Ottawa, Canada, [2]University of Toronto, Toronto, Canada, [3]Canadian Partnership for Stroke Recovery, Ottawa, Canada

Neonatal hypoxia-ischemia (HI) is one of the most common causes of mortality and morbidity in children, often leaving survivors with profound physical and cognitive disabilities. Effective treatments capable of supporting long-term recovery and reducing the severity of these disabilities are needed. Previous research using adult animal models of stroke has shown that metformin, an antidiabetic drug, promotes neurogenesis, oligogenesis and angiogenesis to enhance motor and cognitive function following injury. This study aims to determine whether metformin, enriched rehabilitation (ER) or a combination of the two could provide a clinically relevant therapeutic option for enhancing motor function following neonatal HI.

At post-natal day (PND) 7, Sprague-Dawley rats were assigned to two groups: sham (n=7) or hypoxia-ischemia (n=22). The Rice-Vannucci model was used to induce unilateral injury, in which HI animals had their left carotid artery permanently ligated prior to being placed in a hypoxia chamber (8% O2) for 90 minutes. At weaning (PND 21), animals assigned to ER were housed in an enriched environment and received reach training for 4 weeks. All other animals were standard housed. Once weaned, pups received subcutaneous metformin (200mg/kg/day) or saline injections for 4 weeks. Motor function was assessed pre- and post-combined therapy using the following tests: ladder-walking, adhesive-strip removal and Montoya staircase.

Following four weeks of treatment, hypoxia-ischemia animals receiving ER made 45% fewer errors with their impaired forelimb and 17% fewer errors with their impaired hindlimb on the ladder-walking test compared to standard housed HI animals. ER animals also displayed a decreased latency to contact the adhesive strip on their impaired forelimb. In addition, animals receiving either metformin or enriched rehabilitation showed enhanced motor learning on the Montoya staircase.

In conclusion, enriched rehabilitation promoted motor recovery following HI, while both ER and metformin accelerated acquisition of a skilled reaching task. Work in progress is examining the effects of metformin and enriched rehabilitation on cognitive function following HI.

F29: Effects of Limb Non-Use on Resting Functional Connectivity

Alex Carter, Kristi Zinn, Xin Hong

Washington University School of Medicine, Saint Louis, MO, USA

Background: Upper limb weakness is common after stroke, and in the acute phase results from direct damage to the sensorimotor network. However, in the subacute and chronic phases, learned non-use might lead to secondary brain reorganization and further impairment. To gain insight into brain reorganization after limb non-use, functional connectivity (FC) was analyzed using resting state (rs) functional magnetic resonance imaging (MRI) before and after arm immobilization (AI) in healthy subjects. We hypothesized that rsFC is driven in part by a history of coactivation between brain regions. This hypothesis predicts that reduced activity in the motor system will be associated with specific decreases in rsFC between regions involved in reaching, grasping and motor control.

Methods: Thirteen young healthy subjects wore a shoulder immobilizer that prevented shoulder/arm/wrist extension and flexion most of the day and night for two weeks. Motor performance was assayed before and after immobilization with grip strength, nine hole peg test (NHPT) and finger tapping tasks. RsFC MRI was obtained pre and post immobilization to analyze sensorimotor network reorganization using a seed based analysis. Seeded regions of interest (ROI) included M1, SMA, PMd, putamen, thalamus, insula and multiple regions in posterior parietal cortex important in reaching (superior parieto-occipital sulcus) and attention (intraparietal sulcus). Single pulse transcranial magnetic stimulation (TMS) was used to determine a laterality index of motor cortex excitability between the hemispheres.

Results: AI led to a reduction in grip, NHPT and finger tapping of the left hand. In AI responders, rsFC was decreased between multiple ROIs including the putamen, precuneus, dorsal medial superior parietal lobe, and regions in the posterior parietal cortex involved in reaching and attention. Some increases in rsFC were seen in the right insula. A secondary whole-brain voxel-wise analysis, showed clusters of decreased connectivity between motor and parietal cortex consistent with dorsal attention and default mode resting state networks. Changes in interhemispheric rsFC between left and right motor cortex were correlated with changes in the laterality index of cortical excitability.

Discussion: Two weeks of AI led to significant changes in rsFC between frontal, subcortical and parietal regions known to play a role in planning and execution of arm movements. These changes could represent the neural correlates of learned non-use. The rsFC changes were not purely decreases suggesting that rsFC may not be driven solely by the amount of brain co-activity. Decreased rsFC has been reported with some forms of learning. Adapting to immobilization may involve a degree of motor learning. Therefore we cannot say conclusively that the changes in FC are purely maladaptive or due to non-use. In addition, limb immobilization may lead to reorganization within brain regions beyond the sensorimotor network including regions involved in planning and attention.

F30: Short-Term Practice Effects Predict Longer-Term Upper Extremity Motor Learning in Older Adults With and Without Mild Cognitive Impairment

Sydney Schaefer[1,2], Jeffrey Nielsen[1], Tyson Lumbreras[1], Kevin Duff[2]

[1]*Utah State University, Logan, UT, USA,* [2]*University of Utah, Salt Lake City, UT, USA*

While dose-response studies have suggested that larger doses of neurorehabilitation lead to better outcomes, there may be value in using shorter-term ‘practice effects’ to predict responsiveness to a clinical intervention. Recent work in older adults has demonstrated the utility of practice effects after one week of cognitive training, but has focused primarily on explicit memory tasks. We have begun exploring motor tasks that require implicit memory formation (i.e. procedural learning) that may, in concert, provide a more comprehensive assessment of cognitive function in older adults. The purpose of this study was to compare short-term improvements due to practice on a complex upper extremity motor task between samples of young (n=28) and older (n=29) adults. Within the older adult sample, 55% had cognitive scores below the normative cutoff (Montreal Cognitive Assessment, MoCA). All subjects were free of known neurological or musculoskeletal conditions. We hypothesized that over four practice trials within a single session, the rate of improvement would be greatest for the young adults and smallest for the older adults with cognitive impairment. Performance on each trial was measured as the time to complete the motor task, with shorter times indicating better performance. Analyses of variance (ANOVAs) and correlation coefficients showed, however, that all three groups had comparable rates of improvement, despite having significantly different baseline performances on the motor task itself ($p<.0001$). The young adults completed trial 1 in the shortest amount of time, and the cognitively-impaired older adults took the longest. To test the sensitivity of our motor task in discriminating age and cognitive status, we fit Receiver Operating Characteristic (ROC) curves to baseline data (trial 1) as well as improvement data (normalized change from baseline to trial 4). Although ROC curves moderately discriminated young and impaired subjects based on their baseline performance (AUC = 0.75), they were unable to do so above chance based on the *amount of improvement from baseline* (AUC = 0.55). Collectively our data showed comparable improvement after four practice trials, regardless of age or cognitive status. Moreover, these short-term practice effects were significantly related to 1) the amount of learning achieved by the older adults after completing a much larger dose of practice (150 trials over 3 days) (Spearman’s r=0.49; p=.018), and 2) the amount retained one month later (r=0.41; p=.05). We do acknowledge that the MoCA is a gross measure of global cognition, and does not specifically test implicit memory; thus, despite some of the older adult group presenting with cognitive impairment, they may have relatively intact implicit memory function. Nevertheless, these results provide preliminary evidence of how short-term practice effects may have predictive value in determining responsiveness to longer-term procedural learning interventions in neurorehabilitation.

F31: Differential Effects of Moderate and High Intensity Exercise on Corticomotor Excitability, Intracortical Inhibition and Intracortical Facilitation

Miriam Rafferty[1,2], Samantha Keil[2], Daniel Corcos[1]

[1]Northwestern University, Chicago, IL, USA, [2]University of Illinois at Chicago, Chicago, IL, USA

Background: Single bouts of aerobic cycling have been shown to have an immediate effect on corticomotor excitability, intracortical inhibition, and intracortical facilitation measured with transcranial magnetic stimulation (TMS). The purpose of this study was to determine whether an immediate bout of treadmill walking led to changes in TMS measures, and whether the response was sensitive to intensity dose. Covariates such as prior experience with high intensity exercise and baseline value of TMS measures were examined.

Methods: Twenty-two participants exercised for 30 minutes on two, non-consecutive days. They walked on an incline at a brisk pace with the intensity targeted to 65% and 80% of age-predicted maximum heart rate. They were tested with single and paired pulse TMS before and after exercise.

Results: Following moderate intensity treadmill walking, corticomotor excitability increased as measured by the motor evoked potential (MEP) amplitude, intracortical inhibition increased demonstrated by a lengthened cortical silent period (CSP) duration, and short-latency intracortical facilitation (SICF) increased ($p < 0.05$ for all). Following high intensity walking the responses were reversed: corticomotor excitability decreased as demonstrated by increased stimulus intensity required to elicit a 1 mV MEP, long-latency intracortical inhibition (LICI) decreased, and SICF decreased ($p < 0.01$ for all). There were no changes in short-latency intracortical inhibition following either intensity walking. These differences were not mediated by past participation in high intensity exercise. Discussion: The response following moderate intensity treadmill walking was a net gain in excitability and facilitation, which could put the brain into a more plastic state. In contrast, the reversed effect of high intensity treadmill walking could indicate a decrease in neural plasticity. The apparent contrast between intensities could be due to proposed U-shaped relationships between exercise intensity and specific neurotransmitter activation, cortisol, or cerebral blood flow.

F32: Reduced Ankle Muscle Co-Contraction after Robot-Guided Therapy in Children with Cerebral Palsy

Yi-Ning Wu[1], Yupeng Ren[2,3], Li-Qun Zhang[2,3]

[1]University of Massachusetts Lowell, Lowell, MA, USA, [2]Rehabilitation Institute of Chicago, Chicago, IL, USA, [3]Northwestern University, Chicago, IL, USA

Background and Aim: The majority of children with CP have gait deviations that lead to higher energy expenditure and impact their quality of life. More than half of the gait deviations in children with CP involve impaired ankle motor control as a result of spasticity, contracture, muscle weakness, disturbed neural drives and so on. Combined stretching and active movement training through robot-guided therapy has demonstrated the treatment efficacy in children with spastic CP. The improvement seen in the previous study might be due to many factors such as reduced spasticity, reduced muscle stiffness, and increased extensibility of calf muscle. However the effect of robot-guided therapy on the muscle activation pattern hasn't been reported. The muscle activation pattern can reflect the outcome on central neural drive. This abstract reports changes of dorsi-/plantar-flexor co-contraction during active ankle dorsiflexion after the robot-guided therapy.

Participants: Ten children with spastic CP (five girls, five boys, aged 8 y 3 mo) were recruited. All of the recruited children were above Gross Motor Function Classification System (GMFCS) level III (able to walk independently with our without assistive device). All had considerable ankle spasticity at the time of recruitment. None of them received the botulinum toxin type A injection six months prior to and during the study.

Methods: An 18-session robot-guided therapy program including passive stretching and active movement training were carried out in a research laboratory within a rehabilitation hospital. Each session consisted of ten minutes of passive stretching, twenty minutes of active movement training followed by ten minutes of passive stretching. Before and after robot-guided therapy, muscle activations of tibialis anterior (TA) and gastrocnemius (GM) during active ankle dorsiflexion were recorded by the surface electromyography (EMG). The amplitude of the EMG linear envelope (LE) of each muscle was normalized to the muscle's corresponding EMG amplitude under the maximum voluntary isometric contraction. The co-contraction index (CCI) was derived by the ratio of GM EMG LE amplitude to TA EMG LE amplitude and was presented in percentage. The higher percentage stands for higher co-contraction. Passive ROM (PROM), active ROM (AROM), dorsiflexor and plantarflexor muscle strength, Selective Control Assessment of the Lower Extremity, and functional outcome measures (Pediatric Balance Scale, 6-minute walk, and Timed Up-and-Go) were used to examine the clinical outcomes.

Results: The clinical outcomes were significantly improved after robot-guided therapy as presented in the previous study. The CCI reduced significantly after the robot-guided therapy program from 11.6% (SD= 8.85%) to 9.3% (SD=9.3) with $p= 0.04$.

Conclusions: The findings of reduced muscles co-contraction suggest that the improvement seen in the clinical outcome might be partly due to improved motor control. The participants could activate the targeted muscle (TA) more efficiently with less disturbances of the antagonist (GA) co-contraction.

F33: Comparing Mirror Visual Feedback and Actual Visual Feedback Post Stroke

Qiang Lin[1,2], Viswanath Aluru[1], Daniel Geller[1], David Rhee[1], Sravani Mudumbi[5], Priya Bolikal[4], Eric Altschuler[4], Ying Lu[3], Preeti Raghavan[1]

[1]New York University School of Medicine, New York, USA, [2]the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, [3]NewYork University, New York, USA, [4]University of Medicine and Dentistry of New Jersey, New Jersey, USA, [5]Johns Hopkins University, Maryland, USA

Mirror visual feedback (MVF) is a non-invasive technique where visualization of movements of the unaffected side can potentially stimulate neural circuits on the affected side for enhanced motor performance. MVF has been used in the rehabilitation of upper limb function after stroke; however the mechanisms by which it affects motor control are not yet fully understood. Thirteen subjects between 27-63 years (mean 45.3, SD =13.2), at least 6 months post stroke performed wrist extension movements using a custom-made wrist trainer in two separate experiments. In the unimanual experiment, subjects moved their affected wrist with (1) MVF provided using a mirror reflection of the movements of the unaffected side on the screen in front of them and (2) actual visual feedback (AVF) by looking at the affected side moving. In the bimanual experiment, subjects moved both wrists simultaneously with (1) MVF provided using mirror reflection of the unaffected side in a mirror between the two arms, and (2) AVF by looking at the affected side moving. Motor impairment, wrist kinematics and surface EMG activity of the wrist extensors and flexors were measured. Due to large differences in the Fugl-Meyer scores and baseline wrist kinematics, the subjects were divided into high performance (n=7) and low performance (n=6) groups for further statistical analysis. During unimanual movements, the high performance group showed increased wrist extension with AVF compared to MVF, but used a feedback strategy where the deceleration time of wrist extension was increased. There was no significant difference in EMG activation or co-activation across the wrist flexors and extensors. On the other hand, the low performance group showed no significant differences in wrist extension between AVF and MVF, but also used a feedback strategy with AVF and showed increased wrist flexor, extensor and flexor-extensor co-activation compared with MVF. During bimanual movements, the high performance group used a feedforward strategy with MVF with higher acceleration times compared with AVF, but no other differences in performance were noted. The low performance group, showed lower wrist flexor activation and co-activation with MVF compared to AVF. The results suggest that actual visual feedback from looking at the affected hand moving improves wrist extension using a feedback strategy in the high performance group, whereas mirror visual feedback reduces co-activation in the low performance group which may be helpful to promote easier movement in this group. It is necessary to stratify subjects based on their performance in order to understand motor control patterns and develop evidence-based personalized training strategies post stroke.

F34: Discriminating Visuospatial Neglect from Proprioceptive Impairment using Robotics

Janice E. Yajure[1,2], Jennifer A. Semrau[1,2], Troy M. Herter[4], Stephen H. Scott[3], Sean P. Dukelow[1,2]

[1]University of Calgary, Calgary, AB, Canada, [2]Hotchkiss Brain Institute, Calgary, AB, Canada, [3]Queen's University, Kingston, ON, Canada, [4]University of South Carolina, Columbia, South Carolina, USA

Visuospatial neglect commonly occurs after stroke and results in impaired attention to locations, objects and limbs in contralesional space. Neglect typically leads to increased recovery times and poorer outcomes following stroke. Typically, neglect is identified based on clinical impression which is supplemented with pen and paper assessments, such as the Behavioral Inattention Test (BIT). Our group has previously reported that a high percentage of stroke survivors who perform poorly on the BIT also perform poorly on robotic testing of proprioception. However, we have also seen a number of anecdotal cases of individuals with poor proprioception who appear to be have been misdiagnosed by clinicians as having neglect. We sought to compare the clinician's impression of the presence of neglect in acute stroke subjects, performance on the BIT and robotic proprioceptive testing. Determining specific impairments can guide therapists to deliver targeted interventions.

Hospital charts of 252 subjects with subacute stroke were reviewed to determine whether clinicians (physicians, occupational and physiotherapists) had identified neglect as a presenting symptom on their initial assessment. Subjects were assessed in the research laboratory using the conventional sub-tests of the BIT and underwent robotic assessment of position sense (PM: sense of limb location) and kinesthesia (KIN: sense of movement) on the KINARM exoskeleton . Failure on each of the robotic tests was determined via comparison to the 95% limits of normative control data.

Seventy subjects were determined by clinicians to have neglect versus 56 subjects that were identified as having neglect through the BIT. One-hundred twenty-six subjects failed PM, while 163 failed KIN. The majority of subjects that failed the BIT also had clinician identified neglect (C+, BIT+ N=40). However, 30 subjects identified by clinicians actually passed the BIT (> 129) (C+,BIT-). Many subjects who failed the BIT were not identified by clinicians (C-,BIT+, N=16). We found that nearly all subjects in the C+,BIT+ and C-,BIT+ groups had significantly impaired PM (C+,BIT+=90% N=36, C-,BIT+=75%, N=12) and KIN (C+,BIT+=98% N=39, C-,BIT+=100%, N=16). We found that many subjects in the C+BIT- group had significant proprioceptive impairments (PM=57%, N=17, KIN=73%, N=22). When we compared the proportion of C+BIT- subjects with proprioceptive impairments to those subjects with normal BIT and no clinician-identified neglect (C-,BIT- N = 166, PM=37%, KIN=52%), we found a 20% higher proportion of subjects failing proprioceptive tasks in the C+BIT- group.

We found that many individuals identified by clinicians as having neglect with negative testing on the BIT had significant proprioceptive impairments according to performance on robotic measures of proprioception. We question whether clinicians are misidentifying proprioceptive loss as visuospatial neglect. This speaks to the necessity for better and more sensitive assessments of post-stroke impairments.

F35: Transcranial Direct Current Stimulation Lessens Dual Task Cost in People with Parkinson's Disease

Chad Swank, Jyutika Mehta, Christina Criminger

Texas Woman's University, Dallas, TX, USA

Background & Objective: Parkinson's disease (PD) progressively impairs individuals of cognitive and physical function including walking. Gait for people with PD degrades during motor-cognitive interplay (i.e. dual task conditions). Current management of people with PD improves motor symptoms but inadequately benefits cognitive function, indicating a necessity for novel treatment approaches. Transcranial direct current stimulation (tDCS), a form of noninvasive brain stimulation, may have therapeutic potential as it has demonstrated isolated facilitation of motor and cognitive processing in people with PD. Therefore, our purpose was to identify if application of bilateral brain hemisphere protocol of tDCS improved the ability to divide attention during walking in people with PD.

Design: Participants with PD between 50-80 years received two sessions of tDCS protocol (1 $tDCS_{active}$, 1 $tDCS_{sham}$) during "ON" times separated by 7 days. tDCS protocols were randomized and blinded to participants. Following each tDCS protocol, participants performed single and dual task gait. Gait conditions were randomized.

Setting: Texas Woman's University Human Neurophysiology lab.

Participants: Convenience sample of nine people with PD age 50-80 years.

Interventions: Single 20-minute session of bilateral tDCS (dorsolateral prefrontal cortex; left = anode, right = cathode) at 2mA and one sham session. Participants were seated without a concurrent task during the tDCS protocol.

Main Outcome Measures: Participants were assessed at baseline for disease severity [United Parkinson Disease Rating Scale (UPDRS)] and executive function [Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)]. Following each tDCS condition ($tDCS_{active}$, $tDCS_{sham}$), participants performed Timed Up and Go (TUG) single and dual task conditions (TUG_{alone}, TUG_{motor}, $TUG_{cognitive}$) and Parkinson's Disease Questionnaire - 39 (PDQ-39).

Results: Participants [UPDRS x=38.89 (range=20-60), RBANS x=82.56 (13%ile)] showed no significant differences on paired T-tests for TUG conditions (TUG_{alone} (p=0.39), TUG_{motor} (p=0.41), $TUG_{cognitive}$ (p=0.15)) or PDQ-39 (p=0.32). Gait velocity dual task cost for TUG_{motor} was 22.27% ($tDCS_{active}$) compared to 23.7% ($tDCS_{sham}$) and for $TUG_{cognitive}$ was 28.24% ($tDCS_{active}$) compared to 42.51% ($tDCS_{sham}$). Cognitive dual task cost for $TUG_{cognitive}$ was 13.92% ($tDCS_{active}$) versus 19.79% ($tDCS_{sham}$). Dual task cost was only minimally or moderately related to disease severity (UPDRS; r = 0.049-0.516) and cognitive performance (RBANS; r = 0.058-0.616).

Conclusions: Our bilateral tDCS protocol in participants with PD did not significantly improve dual task gait. However, dual task cost following $tDCS_{active}$ was decreased. Further investigation of our bilateral tDCS approach on dual task gait in people with PD with larger sample size appears warranted.

F36: Characterizing Impairments in Digit Angular Excursion and Individuation in Different Shoulder Positions Post-Stroke

Alvin Tang[1], Viswanath Aluru[1], Mohamed Hassan[3], Lauri Bishop[2], Joel Stein[2], Preeti Raghavan[1]

[1]New York University School of Medicine, New York, New York, USA, [2]Columbia University, New York, New York, USA, [3]New York University Physical Therapy, New York, New York, USA

The ability to move the fingers independently is necessary to perform everyday tasks such as typing, grasping objects of different shapes and playing music. A stroke invariably leads to impaired finger independence particularly for finger extension. It has been suggested that arm posture and orientation can affect finger independence. Here we characterize finger independence in the affected hand in subjects with chronic stroke and determine its relationship to arm posture. Thirteen subjects, 28-81 years, with chronic hemiparesis at least 6 months post-stroke participated in the study. The degree of upper limb motor impairment was assessed using the Fugl-Meyer Scale (FMS). Subjects were asked to perform three 15-second cyclical maximal flexion-extension movements of an instructed finger from the MCP joints of the affected and unaffected hands, while keeping all the other fingers as still as possible in three different shoulder positions: (1) shoulder neutral and elbow flexed to 90 degrees, (2) shoulder flexed to 90 degrees, and (3) shoulder abducted to 90 degrees. The forearm was supported in all three positions. The angular displacement, frequency and distance travelled by the fingers were recorded using an instrumented glove (Cyberglove, Immersion Corp., San Jose, CA). We computed the frequency of finger excursions, the extent of finger flexion and extension, and the individuation index which reflects the degree to which the instructed finger moves while keeping all the other fingers still. The metrics were compared across the three shoulder positions. We found that the frequency of finger excursions and the degree of flexion were greater in the shoulder neutral position across most subjects. The degree of finger extension and individuation varied across individuals: subjects with severe motor impairment (FMS<20) showed greater finger extension and individuation in the shoulder neutral position, whereas subjects with moderate motor impairment (FMS=20-50) showed higher finger individuation and/or finger extension in the shoulder flexed or abducted position. The results suggest that the effect of shoulder position on finger independence depends on the stage of recovery likely due to the effect of arm posture on potentiation of spasticity and synergy patterns. Using shoulder positions that inhibit spasticity may be helpful in training finger individuation and/or extension.

F37: Statin Medication Use and Nosocomial Infection Risk in the Acute Phase of Stroke

Douglas Weeks[1], Christopher Greer[1], Megan Willson[2]

[1]St. Luke's Rehabilitation Institute, Spokane, WA, USA, [2]Providence Sacred Heart Medical Center, Spokane, WA, USA

Background: Statins have immunomodulatory and peripheral anti-inflammatory properties that are independent of their lipid-lowering action. Whether these properties can reduce risk for developing post-stroke infection is debated in clinical literature.

Objective: To estimate the risk for developing nosocomial post-stroke infection based on treatment with statins in patients age 18 or older hospitalized for ischemic stroke.

Methods: In this retrospective cohort study, a consecutive sample of acute care hospital electronic medical records were analyzed. Patients were assigned to the exposed arm when statin use either preceded infection or statins were used, but no infection was reported. Patients not on statins during the hospital stay regardless of infection status and patients initiating statins after infection had occurred were assigned to the unexposed arm. The association of statins with incidence of infection was examined with binary conditional stepwise logistic regression (LR) when post-stroke infection risk factors, namely advanced age, sex, stroke severity, intubation, dysphagia, and presence of other immunomodulatory medications, were controlled. Cochran-Mantel-Haenszel (CMH) analyses examined the association of statin exposure and infection status within strata of each binary LR predictor variable that significantly increased odds of infection.

Results: Records for 1606 patients were analyzed: 1176 in the exposed arm and 430 in the unexposed arm. Infection developed in 18% of the statin exposed group and 35% of the unexposed group ($P < .001$). The adjusted odds from LR for development of infection given treatment with statins was .438 indicating that statins significantly ($P < .001$) reduced odds for developing nosocomial infection by 56% over no exposure to statins. CMH analyses revealed that statins significantly lowered risk for developing infection in males and females and patients with dysphagia. Statins did not significantly reduce risk of infection for patients intubated with either a nasogastric tube or endotracheal tube.

Conclusions: In patients with ischemic stroke and no additional procedure-related risk factors for infection, namely nasogastric intubation or endotracheal intubation, treatment with statins was associated with significantly reduced risk for development of nosocomial infection.

F38: Use of the GesAircraft Video Game for Upper Limb Rehabilitation in Stroke: A Pilot Study

David Putrino[1,2], Helma Zanders[1], Avrielle Rykman[1], Peter Lee[1], Luis Disla[3], Owais Naeem[3], Tanjin Panna[3], Dylan Edwards[1,2]

[1]*Burke Medical Research Institute, White Plains, NY, USA,* [2]*Cornell University, New York, NY, USA,* [3]*GesTherapy, Inc, Brooklyn, NY, USA*

Introduction: Stroke is the leading cause of permanent motor disability in the United States. In the chronic phase of stroke recovery (>6 months post-stroke) more than 60% of stroke survivors still suffer from serious limitations in upper limb functionality. However, this subset of stroke survivors rarely has access to motor rehabilitation at a sufficient intensity to produce meaningful clinical gains due to the cost and inconvenience of regular physical therapy sessions in a traditional clinical environment. Telemedicine is an emerging field that aims to use innovative technology to deliver an unprecedented standard of care to individuals in need. Here we pilot test the feasibility of a telemedicine system designed to improve upper limb function in stroke survivors.

Methods: Our group developed a digital game that utilizes the Leap Motion Controller, an accessible piece of motion-capture technology, to encourage upper limb exercise in stroke survivors. The digital game, called 'GesAircraft', was designed to train three axes of movement: wrist flexion/extension, wrist ulnar/radial deviation and forearm pronation/supination. GesAircraft is capable of automatically calibrating to each user's individual range of motion, allowing for therapy protocols to be personalized to individual ability. Ten stroke survivors who were at least 6 months post- hemorrhagic or ischemic stroke (Mean: 78.4 months; Range: 6-162 months), and with a wide range of upper limb impairment, as assessed using the Fugl-Meyer Assessment (FMA; Mean: 38.8 (17-56). Subjects engaged in 6 weeks of gamified therapy, at a frequency of three sessions per week, and a total of thirty minutes per session. Engagement and usability of the system was assessed using the System Usability Scale (SUS) the Physical Activity Enjoyment Scale (PACES). Following the protocol, the FMA by an independent assessing therapist: to determine whether upper limb impairment had decreased.

Results: Study participants found the system to have "Good" Usability (72±7.9), while clinicians rated the usability of the system as "Excellent" (80±10.2). Participants reported finding the intervention to be enjoyable, with an average response of 5/7 to PACES items. We found no correlation between PACES score and level of impairment. Participants gained 2.8 (±2.1) on the FMA post-therapy, which was determined to be a significant increase ($p<0.001$; one-sample t-test). A significant correlation was also found between increases in the FMA and the participant's PACES score (Spearman's $r^2 = 0.84$, $p < 0.002$).

Discussion: We have demonstrated a system that significantly decreases impairment in chronic stroke survivors following a moderate-intensity exercise protocol. The system is portable, and simple enough to be used independently in the home. The correlation between user enjoyment and treatment efficacy provides us with an interesting insight into how to optimize the efficacy of motor therapy in this population in the future.

F39: Reactive and Voluntary Stepping in Individuals With Stroke: A Comparison Between Paretic and Nonparetic Leg Responses

Chieh-ling Yang[1], Vicki Gray[1], Masahiro Fujimoto[2], Sandy McCombe Waller[1], Mark Rogers[1]

[1]*University of Maryland Baltimore, Baltimore, MD, USA,* [2]*Ritsumeikan University, Kusatsu, Japan*

Background: Fall risk after stroke is a major healthcare concern. Impaired lateral weight transfer between paretic (P) and nonparetic (NP) legs during reactive and voluntary stepping may disrupt balance stability and increase fall risk after stroke.

Objective: We compared the stepping responses of the P and NP leg during unexpected waist-pulls to the P and NP side versus cued voluntary stepping of the P and NP leg in individuals with chronic stroke.

Methods: Fourteen community dwelling individuals >6 months post stroke completed reactive and voluntary lateral step testing. For reactive lateral stepping, 24 trials of randomly-ordered unexpected waist-pull perturbations were applied to the subject (2 directions × 3 repetitions × 4 magnitudes). For voluntary lateral stepping, subjects were instructed to perform 10 trials of a single lateral step as fast as possible according to the direction of a light cue (2 directions × 5 repetitions). The main outcome measures were first step characteristics including step onset, step duration, normalized step clearance, normalized step length in the mediolateral (ML) and anteroposterior (AP) direction, normalized global step length, and normalized center of pressure (COP) velocity. Nonparametric tests were used for comparison of significance between the P and NP leg responses during reactive and voluntary stepping.

Results: During reactive stepping, subjects initiated steps with the NP leg 61 % of the time regardless of the pull direction. Compared to the lateral steps initiated with the NP leg, the P leg steps had a marginally lower clearance (P=0.068), longer ML step length (P=0.068), and shorter global step length (P=0.068). In contrast, during voluntary stepping, all subjects could generate a P voluntary lateral step, however step clearance (P=0.056), ML step length (P=0.026), and global step length were smaller (P=0.056). The AP step length was larger compared to NP stepping (P=0.011). Across the four conditions (reactive lateral steps initiated with P/NP leg and voluntary lateral steps initiated with P/NP leg), a significant difference was found in the first step duration (P=0.031). Post hoc analysis showed a significantly longer step duration in voluntary NP leg stepping compared to reactive NP leg stepping (P=0.046).

Conclusion: We have identified differences between P and NP leg responses during reactive and voluntary stepping in individuals post-stroke. This has implications for the development of rehabilitation interventions to prevent falls in this high risk group.

F40: Towards Assessing Mobility in Parkinson's Disease Patients Using a Single 3D Sensor

Luciano Nocera[1], Helen R. Bacon[2], Jiun-Yu Kao[1], Yu-Chen Chung[2], Yi-An Chen[2], Lorraine Sposto[1], Beth E. Fisher[2], Cyrus Shahabi[1], Carolee J. Winstein[2]

[1]*Integrated Media Systems Center, University of Southern California, Los Angeles, CA, USA,* [2]*Division of Biokinesiology and Physical Therapy University of Southern California, Los Angeles, CA, USA*

For number of disabilities, e.g., Parkinson's Disease (PD), optimized medication and rehabilitation plans require reliable and frequent mobility assessments. Current clinical scales, e.g., the Unified Parkinson's Disease Rating Scale (UPDRS) lack resolution and rely on subjective visual observation. Our Point of Care Mobility Monitoring (POCM2) system uses Kinect to monitor a patient who performs a standardized task. As such POCM2 has the potential to provide an objective assessment solution that can be deployed in the home. We discuss preliminary results of a study where POCM2 was used to characterize the medication state of 14 PD patients, as suggested by the observation that gait in persons with PD can be improved by medication. We report results of a dual-task walking task (i.e., walking in a figure-of-eight pattern while counting backward) for which the Kinect sensor was most accurate while the cognitive task introduces an additional challenge that accentuates the differences between on and off medication conditions. At each timestamp, we considered a subset of 15 nodes (head, neck, torso, shoulders, elbows, hands, hips, knees and feet) of the skeleton that Kinect produces in conjunction with the self-reported most affected side. Steps and strides were automatically segmented (we excluded turns and measurements on segments of the trajectory where the sensor did not have a good viewing angle). Subsequently, steps and strides were used to derive linear and angular kinematic measurements. In the process, post-processing was applied to recover left and right side of the body (Kinect assumes the person is facing the sensor), and limit the maximum extent of joints (Kinect does not constrain joint angles). Each variable was measured multiple times over the course of two trials and the average was used for the statistical analysis. The statistical analysis indicated that left step length and step length grouped by most affected side were both statistically significant ($p<0.05$). For least affected steps, standard deviation of most affected shoulder angle ($p=.003$), least affected shoulder angle ($p=.001$), most affected hip angle ($p=.009$) and least affected hip angle ($p=.002$), and for most affected steps, the average least affected hip angle ($p=.011$), standard deviation of most affected knee angle ($p=.008$), least affected shoulder angle ($p=.001$), most affected shoulder angle ($p=.008$), least affected hip angle ($p=.001$) and most affected hip angle ($p=.001$) were statistically significantly different. These statistical results validate the feasibility of using Kinect to objectively assess the medical state in PD patients. Future work includes completing the study with additional patients to achieve significance for other variables, extending to use additional individual information, using insights from the statistical analysis to inform feature selection for machine learning approaches and extending to use data obtained from wearable sensors to ultimately provide fine grained automated mobility assessment methods.

F41: Rehabilitation-Based Motor Pattern Differences after Biological and Bionic Therapies in Spinal Cord Injury (SCI)

David Logan[1], John K. Lee[1,2], Qi Yang[1], Simon F. Giszter[1,2]

[1]Neurobiology & Anatomy, Drexel University College of Medicine, Philadelphia,PA, USA, [2]Biomedical Engineering, Drexel University, Philadelphia, PA, USA

The goal of this work was to investigate the underlying organization of muscle activations for locomotion during complete SCI (cSCI) rehabilitation. The clinical utility of multi-modal rehabilitation approaches is a growing area of investigation. For example, epidural stimulation (ES) used in combination with rehabilitation training has recently driven improved motor function in patients recovering from severe SCI. Here, we investigate the combined therapies of robot rehabilitation and Adeno-associated viral delivery of Brain-derived neurotrophic factor (AAV5-BDNF) for locomotive rehabilitation following cSCI in a rat model, followed by addition of robot-driven epidural stimulation. We use information-based techniques (i.e., Independent Component Analysis or ICA) to decompose multi-site muscle recordings to examine dimensionality, identify underlying motor modules, and monitor module structure throughout rehabilitation. SD rats (n=3) were implanted with nine intramuscular EMGs in the right hindlimb, from which baseline EMG recordings were made prior to complete transection (T10) and implantation with stimulating electrodes placed on the spinal cord surface (L2 and S2). All rats received AAV5-BDNF microinjections caudal to injury into the ventral horn of the cord, eliciting spontaneous reflex stepping. After recovery, animals were treadmill trained with robotic pelvic rehabilitation therapy (20 min/session) for three weeks, followed by a second phase of robot-driven (as needed) ES for another three weeks. Throughout training, 2 minutes of perineal stimulation was used to elicit strong stepping every other training session. ICA was used to decompose these EMG recordings into informationally distinct underlying motor modules, and to examine the specific contributions of muscles to each of the modules. Weight matrices were compared among sessions across the training period using correlation. These weight matrix correlations revealed distinct groupings across time. First, there were higher correlations in the weeks before epidural stimulation. Spinalized rats initially showed weak local correlations between weight matrices, and intact rat modules, which then strengthened over this period. ES applied subsequently altered these correlations, suggesting a transition in control and modularity occurred between the two rehabilitation phases. The modules no longer correlated as well with intact rats, even after achieving internal stability with a return to high correlations among days achieved in the final two weeks. The modules after ES training correlated less well with the intact rat modules compared to the AAV5-BDNF rehab phase. In sum, contributions of muscle activity to these decompositions appear to be different between the No ES and ES phases of the rehabilitation. These data suggest that early spontaneous locomotive recovery aided by AAV5-BDNF elicits contributions of muscle activations to locomotive recovery that more closely resemble pre-transection patterns than do those observed during ES. Furthermore, dimensionality and muscle contributions alter throughout rehabilitation but different modalities of therapy appear not to elicit the same spinal muscular groupings / activations during recovery.

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F42: Associations Between Foot Cutaneous Sensation and Muscle Activation Patterns During Unexpected Lateral Perturbations After Stroke

Vicki Gray, Chieh-ling Yang, Sandy McCombe Waller, Mark Rogers

University of Maryland, Baltimore, USA

A protective step is commonly used as a strategy to recover and stabilize the body when one's balance is disturbed. After a stroke, balance recovery is difficult with many falls occurring as weight is transferred laterally. Foot plantar sensation may normally be an important sensory input contributing to the sensorimotor control of protective stepping that can be disrupted following stroke. The purpose of this study was to determine the associations between foot plantar cutaneous sensation and muscle activation patterns during protective stepping in response to an unexpected lateral waist-pull to the paretic and non-paretic side in persons with chronic stroke.

Fourteen community dwelling individuals who were > 6 months post-stroke participated in the study. Participants were fitted into a safety harness and were tested using a lateral waist-pull system to induce steps. There were 18 randomly ordered trials and participants were instructed to react naturally and prevent themselves from falling. The electromyographic (EMG) activity was recorded bilaterally from the adductor magnus (AD), gluteus medius (GM), rectus femoris (RF), biceps femoris (BF), tibialis anterior (TA), and soleus (SOL) muscles with surface electrodes during 18 lateral waist-pull trials. Cutaneous sensation was assessed on the plantar aspect of the foot with monofilaments. Correlation coefficients (r) were calculated to determine the strength of associations between the EMG onset and magnitude and cutaneous sensation.

The first recovery step was initiated by the non-paretic leg 63. 4% of the time and 36.6% by the paretic leg. For non-paretic leg stepping, greater impairments in cutaneous sensation of the paretic foot were correlated with an increased EMG area of the GM (r=0.27; p=0.003), RF (r=0.40; p<0.001) and TA (r=0.26; p=0.003) muscles. The EMG area was increased by 27.7% in the GM, 61.4% in the RF and 51.5% in the TA muscles during the first recovery step. For the paretic limb steps, greater impairments in cutaneous sensation were correlated with the initiation time of the AD (r=0.28; p=0.05), GM (r=0.40; p=0.002) and TA (r=0.34; p=0.01) muscles. However, significant differences from the non-paretic limb in the initiation time were only found in the paretic AD (p=0.002) and GM (p=.008) muscles, with a delay of 130 and 110 ms.

The results indicated that persons with more severe sensory impairments of the paretic foot compensate with increased muscle activity when recovering balance with the non-paretic limb. They also, have a delayed onset of muscle activity in the paretic hip muscles when the first step used to recover balance was the paretic leg. This demonstrates the importance of plantarflexor cutaneous sensation and the role it plays in the ability to recover balance from an expected perturbation after a stroke.

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F43: Towards a Low-Cost Alternative for BCI-aided Neurorehabilitation: A Comparison of the Emotiv Epoc to a Clinical EEG System

Camilo Aguilar[1,2], Omar Shanta[1], Thuong Tran[1], David Reinkensmeyer[1], Sumner Norman[1]

[1]University of California, Irvine, Irvine, California, USA, [2]Purdue University, West Lafayette, Indiana, USA

Brain-computer interfacing (BCI) is a form of human-machine interaction with potential to enhance rehabilitation therapy after neurological injuries. The most common method used to capture data in BCI is electroencephalography (EEG). In EEG, electrodes embedded in a non-invasive cap detect electrical signals over the user's scalp. The BCI then decodes these signals to control an external device, such as a wheelchair or exoskeleton robot.

Although EEG has proven useful for neurorehabilitation, typical systems are very expensive, limiting their use to clinical and research settings. In recent years, low-cost alternatives, such as the Epoc by Emotiv©, have targeted widespread use of BCI including bringing BCI into the home.

In this study, we compared the low-cost Epoc headset to a more expensive clinical grade EEG system: the EGI Clinical Geodesic hydrocel. The Epoc consists of 14 dry electrodes and samples at 128 Hz, while the EGI uses 256 electrodes and samples at 1000 Hz. We collected data from six (N=6) unimpaired subjects (4 right-handed, 5 Female) using their left hand to play a musical computer game, similar to Guitar Hero©. Participants received robotic assistance from the Finger Individuated Grasping Exercise Robot (FINGER). We used a two factor, two level factorial design where the factors were robot assistance (on or off) and overt motor activity by the subject (active or passive) resulting in 4 experimental conditions. Participants completed a total of 62 trials in each condition.

We investigated the ability of each EEG system to reliably detect Event Related Desynchronization (ERD), a commonly used signal for BCI-contingent robot therapy. ERD refers to the reduction in amplitude of mu (8-13 Hz) oscillations over the sensorimotor cortex, known to precede both overt and imagined movement.

The more expensive EGI headset detected significant ERD in all subjects and all movement conditions when compared to passive recording (t-test, p < 0.01). The less expensive Epoc detected ERD for only one subject when the participant was active (within-subject MANOVA, p = 0.0383). The magnitude of ERD was also significantly greater with the EGI headset (t-test, active subject, p < 0.01).

The importance of the sensorimotor cortex in neurorehabilitation means that any EEG system used for BCI must reliably detect motor signals such as ERD. The 14 channels of the Epoc do not adequately cover the scalp, most closely approaching sensorimotor cortex with electrodes at F3/F4 and FC5/FC6. It is likely that the Epoc detected ERD in these nearby channels in one subject through volume conduction, as evidenced by the reduction in ERD magnitude. Although the Epoc shows promise in its ability to detect raw EEG, its electrode placement meant it was unable to reliably detect ERD, thus limiting its potential for applications in robotically assisted therapy.

F44: Employing Patient's Individual Characteristics to Derive Personalized Brain Stimulation Therapies

Vishwanath Sankarasubramanian[1], Nicole Varnerin[1], David Cunningham[1], Kelsey Potter-Baker[1], Ken Sakaie[1], Adriana Conforto[2], Andre Machado[1], Ela Plow[1]

[1]Cleveland Clinic, Cleveland/Ohio, USA, [2]Sao Paulo University, Sao Paulo, Brazil

Background: Non-invasive brain stimulation is one of the most well studied advances in stroke rehabilitation. The classical approach focuses on facilitating adaptive plasticity of the damaged hemisphere, particularly the primary motor cortex (M1). However, the promise of stimulation becomes inconsistent when studies include patients with serious damage and disability. In such cases, pathways from M1 are damaged frequently. And, instead, plasticity of alternate substrates in both damaged and intact hemispheres can contribute to recovery. But, how does one identify which substrate to stimulate to precisely affect recovery?

Objective: Since individual substrates offering plasticity vary with damage and disability, we premise outcomes of stimulating these substrates will similarly vary across the range of damage and disability. Comparing their variances will help derive patient-specific substrates for most consistent brain stimulation therapies.

Methods: In a repeated measures crossover design, patients with chronic stroke ranging from mild to severe upper limb impairment received stimulation to facilitate damaged M1 and other damaged and intact substrates, besides sham. Patient characteristics including baseline disability and damage were quantified using scores of impairment and corticospinal integrity. Outcomes were indexed as change in functional reaching ability, and individual expressions of plasticity measured using transcranial magnetic stimulation.

Results: Stimulation rather than sham modulated plasticity and outcomes of paretic upper limb. As predicted, outcomes and plasticity of stimulating different substrates varied differently with baseline impairment and damage. While outcomes of stimulating damaged M1 were robust in patients with mild impairment (r=0.64), the more seriously impaired best responded to stimulation of intact motor cortices (r= -0.812) with cut-offs at mild-to-moderate damage and disability.

Significance: Our findings are consistent with the hypothesis that outcomes of stimulating different substrates vary differently with individual characteristics. The diametrically opposite relationships witnessed between outcomes of stimulating M1 and other substrates could help identify intersection or cut-offs along the range of damage and disability. Cut-offs can stratify patients in which range will benefit from stimulating damaged M1 vs. other substrates for precisely maximizing rehabilitative recovery.

F45: Compensatory Stepping in People with Multiple Sclerosis

Daniel Peterson[1,2], Jessie Huisinga[3], Fay Horak[1,2]

[1]Veterans Affairs Portland Health Care System, Portland, OR, USA, [2]Oregon Health & Science University, Portland, OR, USA, [3]University of Kansas Medical Center, Kansas City, KS, USA

Objective: To characterize compensatory stepping in people with multiple sclerosis (MS) in order to identify possible targets for stepping rehabilitation.

Methods: 54 people with MS and 21 age-matched healthy adults underwent forward and backward support surface translations. Slow- "in-place" perturbations (4cm in amplitude, 15cm/s in velocity) and faster- "stepping-response" perturbations (15cm in amplitude, 56cm/s in velocity) were carried out. Body kinematics and shank electromyography were captured. Persons with MS also completed clinical outcomes including the European Database for Multiple Sclerosis Disability Score (EDMUS-DSS) and 25ft timed walk.

Results: People with MS exhibited more center of mass movement after perturbations and more pronounced deficits in compensatory stepping characteristics than healthy adults (e.g. step latency, number of steps, anticipatory postural responses). Stepping deficits in MS were observed primarily during backward stepping and were correlated to clinical outcomes (EDMUS-DSS; 25ft walk time). Both healthy subjects and persons with MS exhibited slower muscle onset time after fast translations compared to slow translations. Conclusions: Compensatory steps are altered in people with MS, however these deficits are more pronounced during backward stepping than forward stepping which suggests backward stepping may be more effective at identifying stepping dysfunction in MS. Step latency and anticipatory postural responses are particularly altered during backward stepping in people with MS and may be appropriate targets for neurorehabilitation.

F46: Changes in Corticomuscular Coherence Associated with Different Levels of Isometric Hand Force Production Using MEG

Guiomar Niso[2], Sylvain Baillet[2], Elizabeth Bock[2], Patricia da Cunha Belchior[1], Marie-Hélène Boudrias[1]

[1]School of Physical & Occupational Therapy, McGill University, Montreal, Quebec, Canada, [2]McConnell Brain Imaging Centre, Montreal Neurological Institute, Montreal, Quebec, Canada

Introduction: Previous research has shown that 15-30 Hz oscillatory activity in the primary motor cortex (M1) is coherent or phase locked to activity in contralateral hand muscles. This phenomenon has mainly been studied during the production of precision grip task using the index and thumb [1]. In this study, we investigate task-dependent modulation in the coherence between M1 and hand muscles during the production of different levels of grip force, as well as extend this investigation to additional motor areas such as the supplementary motor area (SMA), premotor dorsal (PMd) and premotor ventral (PMv) areas.

Material & Methods: Two healthy female subjects (26 & 41 years old) were scanned while performing hand grips following a hold-ramp-hold pattern with their dominant right hand. We particularly focused on the differences during the three parts of the task: low force hold (3s), ramp (3s) and high force hold (3s). Three different levels of low-high difficulty were analyzed: 10-30%, 20-50% and 30-70% of maximal contraction. Subjects received visual feedback of gripper force levels and were instructed to keep them within target boxes throughout each trial. Surface EMGs were recorded from four forearm muscles: First Dorsal Interossei (FDI), Extensor Carpis Ulnaris (ECU), Flexor Carpi Radialis (FCR), Extensor Digitorum Communis (EDC); and MEG recordings were acquired with a 272-channel CTF system at a sampling rate of 2 kHz. Power spectral density (PSD) using Welch method, Time-frequency (TF) analysis using complex Morlet wavelets, and corticomuscular coherence (CMC) were computed for the different levels of force.

Results:

PSD: MEG sources in M1, SMA, PMd and PMv show clear peaks in the alpha and beta frequency ranges for all force levels. EMG signals also exhibit peaks in the alpha and beta range, the beta peak being more prominent at lower force levels.

TF: M1 and SMA exhibit an increase in beta activity during the holding periods (low and high) that decreases during the ramp period. Similar behaviour was observed for the FDI, ECU and EDC muscle signals, as previously reported [1]. The 20-50% condition exhibited the greater modulation with force.

CMC: An increase in CMC was found in the beta range between MEG and EMG signals during the two holding periods. In particular, M1 and EDC, showed the greatest coherence. This effect diminishes when higher forces were produced.

Conclusion

These results argue in favor of CMC being related to specific parameters of isometric grip force in healthy subjects. These observations will be compared to subjects suffering from stroke and/or other pathological aging processes characterized by motor impairments in a larger subject group.

[1] Kilner et al.,The Journal of Neuroscience, December 1, 2000, 20(23):8838-8845

F47: Distribution of Corrective Movements Differ in People Post Stroke During Paretic Arm Reaching

Clinton Wutzke[1,3], Shashwati Geed[3], Evan Chan[2], Rachael Harrington[3,4], Michelle Harris-Love[3,5]

[1]Veterans Affairs Medical Center, Washington, District of Columbia, USA, [2]MedStar Health Research Institute, Washington, District of Columbia, USA, [3]MedStar National Rehabilitation Hospital, Washington, District of Columbia, USA, [4]Georgetown University, Washington, District of Columbia, USA, [5]George Mason University, Fairfax, Virginia, USA

Following stroke, individuals with severe movement impairments commonly have difficulty reaching. To optimize rehabilitation paradigms to improve reaching movements of people post stroke, it is crucial to characterize how reaching in this population differs from those with more mild movement impairments. Movement units (reversals in tangential velocity of the hand during a reach) have been previously used to describe reaching in people post stroke, however this measure may not fully capture differences between functional groups.

The purpose of this study was to develop a novel analysis technique to describe forward reaching by utilizing the onset of corrective movements in people post stroke. We hypothesized that the distribution of corrective movements in people with severe movement impairment would differ compared to people with mild arm impairment post stroke.

Upper extremity function was categorized by score on the Upper Extremity Fugl-Meyer [UEFM] (Severe: score <30; Mild: UEFM score >35). Twenty-five people post stroke (14 mild UEFM: 52.3+9.7; 11 severe UEFM: 17.8+8.4) completed a forward reach task with the paretic limb. Participants completed forward reaching movements with the paretic arm in response to a visual 'Go' cue to targets located at 80% of their maximum voluntary reach distance.

Reach duration was normalized to one hundred data points for each trial. Movement units were identified by significant positive peaks in x-y (horizontal plane) tangential velocity of the hand. Peaks were considered significant if the height of a peak exceeded 15% of the maximum peak velocity. This analysis included 131 forward reaches by people with mild movement impairment and 99 forward reaches by participants with severe arm movement impairment. Analysis was conducted using custom Matlab programs with a significance level identified a priori at $p<0.05$.

A two-sample Kolmogorov-Smirnov test was used to compare the cumulative distribution functions (CDFs) of movement units throughout time-normalized reach in people with mild or severe impairment. The null hypothesis that movement units in mildly- and severely-affected stroke patients are similarly distributed during reach was rejected (test statistic 0.201, $p = 0.004$). The results indicate the onsets of corrective movements are unequally distributed in time during reaching in people with mild and severe arm impairment post stroke.

These results suggest that people with severe arm impairment initiate corrective movements at the mid-point of the forward reach, suggesting a greater dependence on visual feedback. Individuals with mild arm impairment had greater occurrence of corrective movements in the final 10% of the time-normalized reach suggesting a more smooth velocity profile with a corrective movement to make contact with the target. Further analyses are necessary to describe corrective movements during a forward reach in people with severe arm impairment.

F48: Clinical Characteristics Changes of Phantom Phenomen After Traumatic Limb Amputation

Widjajalaksmi Kusumaningsih

Department of Rehebilitation Medicine, Faculty Of Medicine, University Of Indonesia, Jakarta, Indonesia, Indonesia

Background: The clinical characteristics changes of phantom phenomen after traumatic limb amputation are related to clinical score of referred phantom limb sensation (RPLS) and telescoping measurement.

Objectives: To identify the changing clinical characteristics of phantom phenomen after traumatic limb amputation.

Methods: Fifty limb ampute subjects were included in the study and were allocated in two independent group. Group using prosthetic and group not using prosthetic.

Result: Within six months observation there was an increase in telescoping degree followed by referred phantom limb sensation and lower phantom pain intensity that was statistically significant ($p<0{,}0001$). There was also significant difference between the two group ($p<0{,}0001$).

Conclusions: Changed in clinical characteristics of phantom phenomen after traumatic limb amputation are related to clinical score of referred phantom limb sensation and telescoping. This show the consequence of reorganization of neuroplasticity process. This process was hasten by using functional prosthetic.

Keyword: Neuroplasticity, Phantom limb, Telescoping, Referred Phantom Limb Sensation

F49: Electrophysiological Mechanisms Underlying Visual Feedback in Prism Adaptation

S.J. MacLean[1], O.E. Krigolson[2], G.A. Eskes[1]

[1]Dalhousie University, Halifax, Nova Scotia, Canada, [2]University of Victoria, Victoria, British Columbia, Canada

Background: Prism adaptation (PA) is a promising rehabilitation tool for visuo-spatial neglect. Not everyone with neglect responds to PA, however, nor do PA after-effects always generalize to functional tasks. Therefore, a better understanding of the underlying neural mechanisms of PA may be useful to decompose the important processes underlying PA and to optimize PA effects for clinical use. We recently showed that two event-related potentials (ERPs) are evoked by feedback during PA in healthy controls: the error-related negativity (ERN) and the P300. ERP research suggests that the ERN reflects a mid-frontal error processing system responsible for immediate behavioural corrections and the P300 comprises a more posterior "context-updating" system signaling revisions to participants' working model of the environment, but their role in PA is unclear. Purpose: To investigate whether these ERP components play a role in producing PA aftereffects. Thus, we evaluated these components during PA in response to different types of visual feedback that are known to modulate strength of after-effects. Method: Healthy young adults wearing prism glasses performed memory-guided reaches towards vertical line targets spanning a touchscreen. There were three between-subject feedback conditions at screen touch: (1) view of both hand and target (i.e., target reappeared at screen touch), (2) view of hand only (i.e., target did not reappear), or (3) view of target only with a second vertical line to mark hand position (i.e., reaching was performed under an occlusion board). We compared ERPs evoked by onset of these different feedback events as well as the size of their respective after-effects.

Results: Feedback with view of hand, both with and without explicit target, led to stronger after-effects (mean error = 5.3° and 5°, respectively) compared to target only feedback with hand position marker (mean PVSA error = 1.8°). Parallel to the size of the after-effects, only feedback conditions involving direct view of the hand evoked a P300 component which decreased in amplitude as adaptation proceeded. In contrast, the ERN was seen only when feedback conditions included the target location, even when after-effects were small or minimal. Conclusions: Given that view of hand produced stronger aftereffects, the P300 component may thus serve as a marker of visuo-motor "realignment" processes that are critical to producing strong aftereffects, while the ERN may reflect a neuro-cognitive process related to strategic recalibration. Furthermore, because the P300 amplitude is maximal at parietal-central electrode sites, these data are consistent with imaging studies suggesting involvement of posterior/parietal lobe areas in PA effects. Further study of the role of these components in PA in individuals with neglect is ongoing.

F50: The Control of Grasp Force for Individuals Who Suffered a Stroke and Age-Matched Controls

Charlie E. Anderson, Rajiv George, Vicky Pardo, Kumar Rajamani, Diane E. Adamo

Wayne State University, Detroit, MI, USA

Introduction: Stroke survivors have difficulty overcoming deficits associated with grasping ability that may differ for their right and left hand. The purpose of this study was to determine right and left hand differences in control of grasp force for right handed individuals who suffered a stroke and compare findings to age-matched right handed controls.

Methods: Three groups of participants (22 right hemisphere damage, 20 left hemisphere damage, 23 controls) completed clinical assessments and performed hand-grasp tasks using Instrumented Strain Gauges embedded with force sensors. Pre / post stroke hand preference scores were obtained using the self-reported Edinburgh Handedness Inventory (EHI). A right and left hand reference force was based on 20% of the respective right and left maximum grasp force and provided the reference when matching with the same and opposite hand. Visual feedback, represented by a horizontal line on a computer monitor, displayed the 20% reference force. The matching force, performed without visual feedback, indicated whether the participant overshot or undershot the reference force and this value quantified the Constant Error.

Results: Pre and post EHI scores for individuals with right hemisphere damage were 0.89 / 1.00 and 0.85 / 1.00, respectively indicating they continued to use the right hand for most tasks. Pre and post EHI scores for individuals with left hemisphere damage were 0.87 / 1.00 and 0.53 / 1.00, respectively indicating less right hand use post stroke. For grasp force matching, the ANOVA showed a significant three-way interaction for matching hand x condition x group, $F_{(4,132)} = 8.9$, $p < 0.05$) for constant error. Individuals with right hemisphere damage showed left hand matching undershoots for right hand reference forces ($p < 0.05$) and right hand matching overshoots for left hand reference forces ($p < 0.05$). Similar directional differences were found in the control group. However, those individuals with left hemisphere damage showed right and left hand overshoots for opposite hand matching ($p > 0.05$).

Discussion: Shifts in handedness scores and the magnitude of directional differences in force matching performance were dependent on lesion location. The control group performed in a manner similar to individuals with right hemisphere damage. Those with right hemisphere damage also continued to use their right hand to perform everyday tasks post stroke. Less direct damage to the left hemisphere in people with left hemiplegia suggests that participants continue to use well-learned right-handed movement patterns. However, those with left hemisphere damage showed significantly less right hand use and consistently overshot right and left reference forces. From a clinical perspective, stroke survivors may not be aware of how shifts in hand use or changes in the control of grasp force influence their ability to perform everyday tasks. Further investigation is warranted.

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F51: Validation of Reaching Movements Made in a 2D Virtual Environment in Typically Developing Children

Maxime Robert[1,2], Krithika Sambasivan[2], Mindy F. Levin[1]

[1]Integrated Program in Neuroscience, McGill University, Montreal, Quebec, Canada, [2]Center for interdisciplinary research in rehabilitation of greater montreal, Montreal, Quebec, Canada, [3]School of Physical and Occupational Therapy, McGill University, Montreal, Quebec, Canada

The ultimate goal of rehabilitation is to improve movement kinematics which can be described at two levels: movement quality and motor performance. Measurement of change in movement quality and performance over time is also a method to identify motor learning. Motor learning is based on different principles which can be manipulated in treatment interventions by a therapist or through the use of interactive computer technology, such as virtual reality. Our aim was to compare the kinematics of movements in a physical environment to a similar virtual environment in typically-developing children. Participants (children; 8-17yrs) completed the Edinburgh Handedness Inventory to identify the dominant arm. They practiced reaching in the virtual environment to become familiar with the task. Then, they performed a series of 3 gestures (frontal, vertical and sagittal arm movements) in two environments: virtual and physical environments for a total of 6 gestures. 3D movement kinematics of the arm and trunk were recorded with 6 wireless electromagnetic sensors (G4, Polhemus, Vermont, 120Hz). Participants completed 15 trials of each gesture in each environment (45 trials per environment, for a total of 90 trials). The virtual environment consisted of an interactive game controlled by arm and hand movements (Jintronix, Montreal) projected on a computer monitor. Movements throughout the arm workspace were recorded with a Microsoft Kinect camera and projected into the game scene. Movements made in the virtual environment were less precise, slower and shorter in comparison to those made in the physical environment. In the virtual environment, participants used less trunk displacement in comparison to the physical environment. There were no significant differences between the two environments with respect to the range of motion of the elbow and the shoulder. Differences between movements made in each environment can be explained by less precise body position tracking in the virtual environment, decreased quality of the visual scene and differences in depth perception cues. The overall similarities of movements made in the two environments suggest that training in 2D game-like virtual reality environments may be feasible for motor rehabilitation of children.

F52: Alterations in Cortical Laterality Among Individuals at Risk for Stroke: A Functional MRI Study in Controls and Patients

Daniel Lench, Christopher Austelle, Colleen Hanlon

Medical University of South Carolina, Charleston, USA

Background: It is well-known that the first year after a stroke is a dynamic period for brain recovery. One of the hallmarks of this period is that stroke patients begin to use both the left and right hemisphere motor circuitry to perform a unimanual task (which typically involves a lateralized set of motor structures). Although this pattern may be positive during acute stroke recovery, chronic stroke patients that are unable to restore the typical pattern of lateralized activity often have the worst outcomes. The goal of this study was to test the hypothesis that this bilateral activity is actually present before the stroke in individuals at risk for stroke - and may reflect an early pre-stroke adaptation to their risk factors (high blood pressure, diabetes).

Methods: Functional MRI data and a comprehensive battery of motor assessments were acquired from 22 individuals - a cohort of 11 chronic stroke patients with upper extremity weakness (and 11 participants at-risk for stroke (at least 2 cardiovascular risk factors). During the neuroimaging session, the participants performed a squeezing task with their left and right hands (30 second blocks of left, right, or rest). Percent BOLD signal change was extracted from the caudate, pallidum, precentral gyrus, putamen, SMA and thalamus during the hand pulsing task and rest.

Results: These preliminary data were compared with a previous cohort of individuals that did not have these risk factors. As expected precentral gyrus percent signal change increased when using the contralateral hand in controls. The laterality index in the at-risk participants was lower (less lateralized) than the healthy control, but it was not as low as in the stroke patients. This was particularly true in the cortical areas including the motor and premotor corticies.

Conclusion: These data suggest that there is a high degree of variability in the laterality indicies among individuals that have not had a stroke. It is possible then that some of these premorbid patterns may account for the lack of "relateralization" that is observed many chronic stroke patients.

F53: Avoidance Strategies in Response to Animate and Inanimate Obstacles in Young Healthy Individuals Walking in a Virtual Reality Environment

Wagner Souza Silva[1,2], Gayatri Aravind[1], Samir Sangani[3], Anouk Lamontagne[1,2]

[1]McGill University, School of Physical and Occupational Therapy, Montreal, Quebec/QC, Canada, [2]McGill University, Integrated Program in Neuroscience, Montreal, Quebec/QC, Canada, [3]Feil and Oberfeld Research Center, Jewish Rehabilitation Hospital, Laval, Quebec/QC, Canada

Many studies have described obstacle avoidance strategies while walking, either in physical or virtual environments. These studies, however, were limited to the avoidance of inanimate objects (e.g. cylinders) or failed to address the influence of the visual and auditory properties of the obstacle in shaping avoidance strategies. This study aims to describe the extent to which three different types of obstacles (cylinder, visual human-like avatar and visual human-like avatar with footsteps sounds) affect the inherent avoidance strategies in young healthy individuals. Healthy young adults (n=4, 50% male, aged 24.7 ±3.5 years (mean ±1SD)) were tested while walking over ground and viewing a virtual environment (VE) displayed in a helmet mounted display (HMD) unit (nVisor SX60). The VE, controlled in Caren-3 (Motek medical), simulated a large room that included a target located 11m straight ahead. In addition, three identical obstacles were positioned 7m ahead in three locations facing the subject (40° right, 40° left, and straight ahead). As the subjects walked 0.5m, one of the three obstacles approached them by walking/moving towards a theoretical point of collision located 3.5m ahead at the midline. Meanwhile, the two remaining obstacles moved/walked away from the participants. The ability of the subjects to steer toward the target while avoiding the obstacles was characterized using the 3D position and orientation of the head recorded from reflective markers (Vicon) placed on the HMD. Preliminary findings show a trend towards smaller minimal distances in all directions when interacting with human-like avatars (left: 1.25±0.47; center: 1.22±0.20; right: 1.31±0.24) as compared to cylinders (left: 1.49±0.26; center: 1.29±0.12; right: 1.52±0.17). The addition of footstep sounds to human-like avatars did not modify minimal distance values compared to when no footstep sounds were provided (left: 1.20±0.39; center: 1.71±0.14; right: 1.31±0.28). Onset times of avoidance strategies were similar across all conditions. These findings suggest that participants had equivalent movement perception of the obstacles regardless of the condition displayed. They also indicate that smaller clearances in the presence of human-like entities may occur due to an inherent real life perception of the avatars resulting in actions that rely on strategies applied during daily locomotion. Finally, the similarity of results following the addition of footstep sounds to the visual human-like avatar condition suggests that avoidance strategies may primarily rely on visual cues.

Key Words: Navigation; Vision; Walking.

F54: Muscle Fatigability and Subsequent Torque Decline During Isometric and Isokinetic Knee-Extension Generated by Sequential Electrical Stimulation

Austin Bergquist[1], Vishvek Babbar[1,2], Saima Ali[2], Milos Popovic[1,2], Kei Masani[1,2]

[1]Toronto Rehabilitation Institute, University Health Network, Toronto, Ontario, Canada, [2]Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Ontario, Canada

Background: Functional electrical stimulation is used in rehabilitation to generate muscle contractions and is conventionally applied using a single active electrode (Single-Electrode-Stimulation; SES). During SES, muscle fibres are activated in synchrony with each stimulation pulse, resulting in the need of unnaturally high stimulation frequencies to generate functional contractions. High stimulation frequencies result in high muscle fatigability and rates of torque decline, negatively impacting benefits of rehabilitation involving electrically stimulated muscle contractions. To address this issue, researchers have "spatially distributed" and "sequentially" interleaved stimulation pulses between multiple active electrodes (Spatially-Distributed-Sequential-Stimulation; SDSS). SDSS allows muscle fibres to be activated in an asynchronous manner, reducing the stimulation frequency at each active electrode, while maintaining activation of the muscle as a whole. Although SDSS has been shown to reduce fatigability and subsequent torque decline of isometric contractions, this method has not been tested under non-isometric conditions, as occurs routinely in rehabilitation.

Purpose: To reproduce previous findings that SDSS can reduce fatigability and subsequent torque decline of isometric contractions, and to extend this line of inquiry to isokinetic conditions.

Methods: Ten healthy volunteers participated in 2, 2-hr, experimental sessions. Intermittent stimulation (0.3-s on : 0.7-s off; 120-s total) was delivered to the knee-extensors using SES (1 active electrode; 40 Hz) and SDSS (4 active electrodes, each stimulated at 10 Hz; composite 40 Hz stimulation) in separate trials, to generate isometric (0°/s) and isokinetic (180°/s) torque. Isometric and isokinetic contractions were tested on separate legs in separate trials. A rest period of 72-hr was provided between repeated testing of each leg. Protocol order was randomized. Stimulation intensity was set to generate ~80% of maximum tolerated stimulation current. Measures of fatigability included fatigue index (average peak torque of last 10 contractions ÷ average peak torque of initial 10 contractions) and torque peak mean (average peak torque of all 120 contractions ÷ average peak torque of initial 10 contractions). Data are reported as mean ± standard deviation and were tested using paired t-tests. Significance was set at $P<0.05$.

Results: Fatigue indices were significantly higher for SDSS than SES during isometric (SES = 0.63±0.09; SDSS = 0.79±0.15; P = 0.002) and isokinetic (SES = 0.67±0.14; SDSS = 0.80±0.18; P = 0.001) contractions. Torque peak mean values were significantly higher for SDSS than SES during isometric (SES = 0.79 ± 0.05; SDSS = 0.89 ± 0.08 P < 0.001) and isokinetic (SES = 0.81 ± 0.11; SDSS = 0.87 ± 0.14) contractions.

Conclusion: Presently, we have reproduced previous findings that SDSS reduces fatigability of isometric contractions compared to similar sized contractions generated by SES. Further, we have extended these findings to isokinetic conditions. The present findings are important for understanding the utility of SDSS for use in rehabilitation.

F55: Subcortical Influences on Paired-pulse TMS-induced I-waves in Humans

John Cirillo[1,2], Monica Perez[2,3]

[1]University of Auckland, Auckland, New Zealand, [2]University of Pittsburgh, Pittsburgh, PA, USA, [3]University of Miami, Miami, FL, USA

Paired-pulse transcranial magnetic stimulation (TMS) of the human motor cortex results in consecutive facilitatory motor evoked potential (MEP) peaks in surface electromyography, allowing the possibility to make non-invasive inferences about the physiology of indirect (I) waves. Using paired-pulse TMS over the hand motor cortex of intact humans and individuals with incomplete cervical spinal cord injury (SCI), we examined early (first) and late (second and third) MEP peaks in a resting finger muscle. In uninjured subjects, we demonstrate a reduced amplitude and duration of the third peak compared with the second, irrespective of test (S1) intensity. A higher conditioning (S2) intensity increased the amplitude of the third but not second peak. No difference in amplitude and duration was found between the first and second peaks. A threshold electrical S2 over the cervicomedullary junction facilitated the second and third but not the first peak similarly to TMS. In SCI subjects, we found a decreased amplitude for all MEP peaks compared with controls. The onset of the second and third peaks were delayed, with the third peak also showing an increased duration. The delay of the third peak was smaller than in controls at a lower stimulation intensity, suggesting lesser influence of decreased corticospinal inputs. A mathematical model showed that the third peak aberrantly contributed to spinal motoneurone recruitment after SCI, irrespective of motor unit threshold. Additionally, temporal and spatial aspects of late peaks in SCI subjects correlated with MEP size and hand motor output. Our results indicate that TMS-induced MEP peaks undergo distinct modulation after SCI, with the third peak likely reflecting a decreased ability to summate descending volleys at the spinal level. We argue that subcortical pathways contribute to late TMS-induced peaks in humans with and without SCI.

F56: Memantine Treatment for Post-stroke Aphasia: A Case Control Study

Jennie Valles, Juliana Kennedy, Mery Elashvili, Carolin Dohle

Burke Rehabilitation Hospital, White Plains, NY, USA

Objective: To determine if treatment with memantine will improve post-stroke aphasia

Background: Aphasia occurs in 21-38% of stroke victims and is considered one of the more disabling sequelae with significant impact on cognition and communication. Currently, conventional speech and language therapy remains the gold-standard rehabilitation method for improvement of these deficits but studies suggest that adjunctive treatment with pharmacologic agents such as memantine may provide additional benefit.

Design/Methods: A retrospective case control chart review study was conducted examining patients admitted for stroke rehabilitation. Subjects included in our study had received a diagnosis of aphasia based on language assessment by speech language pathology. The treatment group was comprised of 26 patients treated with memantine. These patients were compared to a historical control group matched for age, sex, and stroke severity. Data was collected from medical records over a two-year time period. FIM Cognitive and FIM Motor Scores from admission and discharge were used to calculate the average FIM Cognitive Score Gain and the average FIM Motor Score gain. Changes in the individual FIM Cognitive sub-scores for Comprehension, Expression, Social Interaction, Problem-solving, and Memory were also analyzed. A subgroup of patients had completed portions of the Western Aphasia Battery (WAB). These WAB sub-scores were collected from admission and discharge and evaluated for gains in accuracy. The data were analyzed for normality with the Shapiro-Wilk test. For normally distributed date, an independent sample t-test was used to test for statistical significance between the two groups.

Results: There was no significant difference between the treatment and control groups for FIM Cognitive Score Gain and FIM Motor Score Gain (5.31 ± 4.32 vs. 4.42 ± 3.50 and 16 ± 13.94 vs. 15.96 ± 11.06, $p = 0.991$). Further analysis of the individual FIM Cognitive subscores did not yield a significant difference. The WAB subscores showed no significance in gains in accuracy between the two groups (15.97% ± 13.99 vs. 19.05% ± 13%, $p = 0.659$). The scores were also controlled for length of stay. Memantine was generally well-tolerated by both groups.

Conclusion: Memantine treatment showed no statistically significant improvement for patients with post-stroke aphasia based on FIM Scores for Motor and Cognition and components of the WAB. Long-term follow-up and larger study groups, however, could provide additional information which may warrant further exploration into the benefits of memantine. A limitation of our study is the small sample size, highlighting the need for collaboration across multiple research sites in order to allow for collection of data from more patients in order to be adequately powered. Such a system would be of great clinical importance for answering simple, but important research questions that can inform the way we provide rehabilitation.