## O1: EEG-informed Machine Learning of Movement Primitives for Neurorehabilitation Robots

Neelesh Kumar, Mona Rassouli, Karansingh Banga, Konstantinos Michmizos
*Rutgers University, Piscataway, USA*

Decoding the fundamental components of movement using brain activity is an important step for not only versatile and robust brain-computer interfaces, but also for faithfully quantifying motion characteristics in real-time and integrating them into adaptive rehabilitation strategies. This adaptation resulting from artificial learning when combined with brain plasticity (biological learning) has the potential to accelerate motor recovery.

Here, we explored the fascinating possibility that a neural network, when designed and trained upon the brain's constraints, has enough discriminative power to predict brain states associated with the movement primitives. We propose a data-driven computational framework wherein we designed and developed a state-of-the-art 3D convolutional neural network, driven by the EEG activity, to decompose movement into its fundamental components namely, the intent of the user to move, the direction of the movement as well as the reaction time. We train this neural network on the dataset collected from an IRB-approved in-house experiment where 13 human subjects performed a goal-oriented motion task during their interaction with our Bionik InMotion Arm robot, informed by our 128-channel Biosemi ActiveOne EEG recording system. The motion task comprised of subjects moving a pointer on the screen to the target box. The experiment consisted of two modes- active (where subjects performed the motion), and passive (where motion was performed by the robot). Our model significantly outperformed the other state-of-the-art models and achieved a mean accuracy of 66.1% on directions (4-classes), 60.6% on reaction-time (2-classes) and 73.3% on active-passive (2-classes) [using 5- layer 3d CNN with ReLU non-linearities, 210 trials per subject, evaluated using leave-one-out technique].

Our results show that deep neural networks conditioned on brain signals can be used to decompose movement into its fundamental components. Through the use of the data-rich brain-constrained deep model to objectify motion characteristics, the pathophysiological movements can be accurately and precisely identified and can be used to optimize therapy provided by the neurorehabilitation robots as they steer these movements towards normalcy.

## O2: Residual Ruins: The effect of spinal cord injury edema on potential functional recovery

Alondra Medina, Alyssa Canales, Kelsey Baker
*The University of Texas Rio Grande Valley, Edinburg, USA*

### Background:

Spinal cord injuries affect about 300,000 individuals in the United States and cause varying degrees of motor and sensory impairment. Currently over 9 months of rehabilitation are often required to achieve meaningful improvements in function in patients with spinal cord injury (SCI). In order to improve rehabilitative efforts for those with SCI, it is critical to identify biomarkers that could serve as indicators for those who would respond to standard rehabilitation efforts. Recent work has suggested that physical properties of the edema that forms around the area of injury in the spinal cord may be one such biomarker. Therefore, the objective of our project was to determine if the properties of the residual edema in the spinal cord after SCI influenced functional recovery.

### Methods:

T2-weighted MRI images were collected in eight subjects with cervical SCI (C2-C7). Following MRI collection, all patients participated in two weeks of rehabilitation. We assessed changes in motor function before and after rehabilitation using the nine-hole peg test and muscle grading. We chose to define the physical properties of the edema using FSLview. We assessed the length, size and location of the edema as well as the volume of residual tissue on the ventral and dorsal side of the edema, termed tissue bridges. Properties of the edema were related to functional recovery metrics using regression analysis. Statistical Package for the Social Sciences (SPSS) software was used for all statistical comparisons.

### Results:

We observed varying sizes of edema and tissue bridges in our patient population. Edemas varied in size from 33.2 mm3 to 2978.5 mm3 while tissue bridges varied in size from 0.081 to 4.06 mm3 in the dorsal region and 0.188 mm3 to 2.28 mm3 in the ventral region. In most subjects, edema spanned two vertebrae levels, with a maximum of six levels observed. We identified that subjects with a larger edema demonstrated reduced baseline function ($r=0.542$) and limited functional recovery ($r=0.297$). In addition, subjects with a larger ventral tissue bridge showed increased baseline function, as defined by the ASIA impairment scale. Ventral tissue bridge volume was also positively related to gains in total strength ($r=.952$, $p=.003$) and distal strength ($r=.930$, $p=.007$).

### Conclusion:

Overall, our work has found that properties of spinal edema and tissue bridges are directly related to baseline function and recovery potential. Our findings encourage future research to evaluate mechanisms to improve tissue bridges in spinal cord injury patients in order to improve recovery.

## O3: Emotion recognition impairments after right-hemisphere stroke – an important factor for long-term outcomes?

Anna Greenwald[1], Katherine O'Connell[2], Abigail Marsh[2], Alexander Dromerick[3]
*[1]Georgetown University Medical Center, Washington, DC, USA. [2]Georgetown University, Washington, DC, USA. [3]MedStar National Rehabilitation Hospital, Washington, DC, USA*

### Background:
Stroke, especially to the right hemisphere (RH), can significantly impair the stroke survivor's ability to recognize and express emotions (Borod et al., 1998; Spalletta et al., 2001; Yuvaraj et al., 2013). In acute stroke, RH dysfunction is better predicted by emotional prosody impairments than by hemispatial neglect (Dara et al., 2014), and caregivers report the stroke patients' apparent loss of empathy as the most important problem after RH stroke (Hillis & Tippet, 2014).

### Objective:
Given the highly plausible link between the ability to read and express emotions and maintaining social support, and given the known importance of social support for health, functional status, and stroke recovery (Steinbach, 1992; Glass et al., 1993; Eslinger et al., 2002), we aim to investigate the potential role of emotion recognition impairments in determining long-term outcomes for RH stroke survivors. In addition, we explore whether functional brain reorganization could aid recovery of emotion recognition ability after stroke.

Specifically, we address the following questions:
1) Are emotion recognition impairments evident in chronic RH stroke?
2) How does emotion recognition ability relate to social outcomes?
3) Is there evidence of functional brain reorganization if the stroke damages those areas normally involved in emotion recognition?

### Methods:
We assessed 20 survivors of unilateral ischemic stroke to the RH and neurologically healthy controls matched for age, sex, race, and SES using the multimodal Geneva Emotion Recognition Test (GERT-S, Schlegel & Scherer, 2016) and the Activity Card Sort (ACS; Baum & Edwards, 2008). A subset of the participants also underwent functional magnetic resonance imaging (fMRI) while performing a vocal emotion recognition task.

### Results:
RH stroke survivors performed significantly worse on the GERT-S than matched controls, and there was a moderate positive correlation between GERT-S scores and the proportion of social activities retained after the stroke. Importantly, the pre-stroke social activities reported by the stroke survivors did not differ from those reported by matched controls, and there was no correlation between emotion recognition ability and pre-stroke social activities.

Functional MRI revealed strongly right-lateralized activations in controls, whereas some of the stroke survivors showed activation in homotopic areas of the left hemisphere.

### Conclusions:
The behavioral results support the idea that emotion recognition impairments after stroke negatively affect social outcomes, although additional research is needed into the moderating effects of factors such as lesion size and general cognitive status. The fMRI findings of functional reorganization to homotopic areas of the opposite hemisphere are reminiscent of the RH activation sometimes observed in LH stroke survivors with aphasia during language tasks (Turkeltaub et al., 2011). This suggests these homotopic areas as potential targets for future interventions aiming to recover emotion recognition by combining behavioral training with neurostimulation, as is currently being investigated for aphasia recovery.

## O4: Effects of Timing and Sex on Neuroprotective Efficacy of Remote Ischemic Conditioning in a Rat Stroke Model

Matthew McDonald[1,2], Angela Dykes[1,2], Matthew Jeffers[1,2], Anthony Carter[2], Ralph Nevins[1], Gergely Silasi[1,2], Dale Corbett[1,2]

*[1]University of Ottawa, Ottawa, Canada. [2]Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, Ottawa, Canada*

Remote ischemic conditioning (RIC), an exercise mimetic, is a non-invasive procedure where blood flow is repetitively reduced in a limb in order to protect a more distal organ (i.e. the brain). RIC delivered before (pre-RIC) or after (post-RIC) stroke is reportedly neuroprotective in preclinical studies. However, these studies have exclusively used male rats, hyper-acute post-stroke delivery times, and the middle cerebral artery occlusion (MCAO) model. Both the Stroke Therapy Academic Industry Roundtable (STAIR) and the Stroke Recovery and Rehabilitation Roundtable (SRRR) emphasize that prior to clinical translation, interventions must be evaluated in multiple stroke models, both sexes, and at clinically feasible times. As such, the objective of this study was to address these weaknesses in the literature regarding the neuroprotective efficacy of RIC. In both male and female Sprague-Dawley rats (n=83) a standardized RIC session (4 repetitions, 5 minute inflation, 5 minute deflation) was delivered to the contralesional hindlimb either before (18 hours) or after (4 hours) endothelin-1 (ET-1) stroke. Infarct volume was assessed using MRI 24 hours after stroke and rats were divided into groups based on stroke size (small vs. large) through hierarchal cluster analysis. Importantly, ET-1 produced smaller strokes more comparable to injury sizes observed clinically (5.2% to 18% of hemisphere) than MCAO models. The RIC protocol provided neuroprotection in both small (mean $42mm^3$) and large (mean $146mm^3$) stroke groups, reducing stroke volume by 35% ($p<0.00001$; $d=0.29$) and 39% ($p<0.01$; $d=1.41$), respectively. The timing at which RIC was delivered also had a significant effect on reducing stroke volume. Pre-RIC reduced infarct volume by 41% ($p<0.0001$, $d=0.92$), while post-RIC reduced infarct volume by 29% ($p<0.01$; $d=0.43$). In regards to sex-specific differences, RIC was more effective in male rats. Specifically, infarct volume was reduced 46% in males ($p<0.0001$; $d=0.94$) compared to a 23% reduction in female rats ($p<0.05$; $d=0.42$). In summary, RIC provided neuroprotection in a translational stroke model and across stroke sizes, but its efficacy was timing and sex-dependent. In accordance with STAIR and SRRR guidelines, this study expands previous preclinical evidence for RIC, and provides more compelling evidence for translation of RIC as a preventative measure or adjunctive treatment prior to hospital arrival, or shortly after stroke.

## T1: Effects of Remote Limb Ischemic Conditioning in Conjunction with Rehabilitation Training After Acute and Chronic Motor Cortical Infarcts in Rats

Bryan Barksdale[1,2], Albert Lee[1], Jill Rosow[1], Mathilda Nicot-Cartsonis[1], Darius Miranda-Sohrabji[1], Theresa Jones[1]
*[1]University of Texas at Austin, Austin, USA. [2]University of Texas Medical Branch, Galveston, USA*

Stroke survivors are often left with chronic disability due to hemiparesis of the upper limb, even after medical and rehabilitation care. Adjunctive therapies that can enhance neuroplasticity during effective motor rehabilitation (RT) is a current focus in the field. One such promising therapy is remote limb ischemic conditioning (RLIC) which is a safe and non-invasive procedure that consists of causing shorts bouts of ischemia to a limb. RLIC has been shown to enhance the learning of motor tasks in healthy adults (Cherry-Allen et al., 2015; 2017; Sutter et al.,2018). However, recent findings suggest that RLIC does not improve motor recovery compared to RT alone in the subacute phase, at least not in middle-aged rats (Barksdale et al., 2018, SfN abstract). The aim of these studies was to determine the effect of RLIC on motor recovery when added to RT during the chronic phase in middle-aged rats and in the subacute phase in young adult rats. Male Long-Evans rats were trained on the single pellet reaching (SPR) task until proficiency was reached and then a surgery was performed to model a cortical stroke by applying endothelin-1 to the caudal forelimb area of the motor cortex. Rats were aged 8 mos in the chronic study and 4-5 mos in the subacute study. RT was started 7 days in the subacute study or 6 weeks post-op in the chronic study and consisted of SPR for 60 trials every day for 14 days. RLIC was administered every 48 hours during RT. RLIC consisted of a blood pressure cuff being applied to the hindlimb and inflated above 200 mmHg for 3 cycles of 5 minutes on and 5 minutes off under isoflurane anesthesia. A control group did not have the blood pressure cuff inflated but was kept under isoflurane for the same amount of time. Ischemia was confirmed by skin temperature drop and/or color change of the hindlimb paw. Performance on the SPR, Schallert Cylinder, and Foot Fault tasks was assessed pre-op, post-op, and post-RT. Current results suggest that RLIC does not enhance motor recovery in the chronic phase of stroke in middle-aged rats. Preliminary data will be presented on the effects in the subacute phase in young adult rats.

## T2: A Robot for Split-Force Body Weight-Supported Treadmill Training Modulates Gait Patterns of Patients with Hemiparetic Stroke: Case studies

Hiroaki Fujimoto[1], Tatsuya Teramae[2], Tomoyuki Noda[2], Asuka Takai[2], Nobukazu Fujita[3], Megumi Hatakenaka[1], Hiramatsu Yuichi[1], Akihiro Jino[3], Jun-ichiro Furukawa[2], Hajime Yagura[1], Teiji Kawano[1,4], Hironori Otomune[1], Jun Morimoto[2], Ichiro Miyai[1]

*[1]Morinomiya Hospital, Neurorehabilitation Research Institute, Osaka, Japan. [2]ATR Computational Neuroscience Labs, Dept. of Brain Robot Interface, Soraku-gun, Japan. [3]Morinomiya Hospital, Dept. of Rehabilitation, Osaka, Japan. [4]Osaka University Graduate School of Medicine, Dept. of Neurology, Suita, Japan*

### Background and aims:

Body weight-supported treadmill training (BWSTT) is expected as an effective therapy to improve poststroke gait disorders. However, conventional BWSTT devices continuously support both sides of the body with identical forces and temporal feature of each leg support in tune with the gait cycle cannot be adjusted to emerge different walking patterns. Thus we have developed a novel robot called “split-force BWS” to support each side of the body separately using pneumatic artificial muscles. We assessed if this robot could modulate the gait patterns of hemiparetic patients with stroke.

### Methods:

Three patients with stroke (three men, 35.3 ± 20.8 years-of-age, 71.3 ± 44.4 days after onset) with mild hemiparesis (lower-extremity Fugl-Meyer assessment score: 29.3 ± 1.5) participated in this study. They were custom-made shoes with load cells and a harness. The robot controls the magnitude of split-force BWS according to the gait cycle under a constant amount of total BWS. It can also set a bias control condition that sets the lower limit of the support force for paretic or non-paretic side during the stance phase. Before the experiment, comfortable walking speed (1.7 to 2 km/hour) at the treadmill and the degree of total BWS (25 to 33%) were set for each patient. In the experimental sessions, patients walked on the treadmill without holding handrails under five modes: 1) no BWS; 2) conventional BWS; 3) split-force BWS without bias; 4) split-force BWS with bias in the non-paretic side; and 5) split-force BWS with bias in the paretic side. We compared the laterality of single stance time (SST ratio = SST of the paretic side/SST of the non-paretic side) among these modes. Behavioral measurements were analyzed using one-way ANOVA. The study protocol was approved by the local ethical committee.

### Results:

There were no adverse events. In two of the three cases, the split-belt BWS with bias mode significantly modulated the SST ratio compared with the no BWS mode ($p<0.05$), while the ratio with conventional BWS did not differ from no BWS mode. The SST of the paretic leg increased under split-force BWS with bias in the non-paretic side compared with the other BWS modes.

### Conclusion:

Split-force BWS was able to modulate gait patterns of stroke patients with mild hemiparesis. Our preliminary results suggest that BWSTT with the split-force BWS robot can provide different walking patterns that cannot be produced by conventional BWSTT devices. Further studies are needed to optimize the training protocol for stroke patients with various severities to improve disorders.

This research results have been achieved by "Research and development of technology for enhancing functional recovery of elderly and disabled people based on non-invasive brain imaging and robotic assistive devices", the Commissioned Research of NICT.

## T3: Increased Sensorimotor Inter- and Intrahemispheric Functional Connectivity is Associated with More Impaired Sensorimotor Upper Limb Function in the Subacute Phase Post Stroke

Nele De Bruyn[1], Leen Saenen[1], Liselot Thijs[1], Eva Ceulemans[1], Sarah Meyer[2], Kaat Alaerts[1], Geert Verheyden[1]
*[1]Department of Rehabilitation Sciences, KU Leuven - University of Leuven, Heverlee, Belgium. [2]Jessa Hospital, Rehabilitation Campus Sint-Ursula, Herk-de-Stad, Belgium*

### Background:

More than 50% of subacute stroke patients suffer from sensorimotor impairments in the upper limb. Disturbed interhemispheric balance and hyperactivity of the contralesional hemisphere within the sensorimotor network is reported to be associated with more severe sensorimotor impairments. However, the effect of stroke on the non-impaired hemispheric functional connectivity related to sensorimotor upper limb function needs to be further explored.

### Aim:

To explore the relationship between altered functional connectivity and sensorimotor upper limb function in the subacute phase post-stroke.

### Methods:

We obtained a resting-state functional magnetic resonance imaging (rs-fMRI) and clinical sensorimotor profile for nine subacute stroke patients and nineteen age-matched healthy controls. Fugl-Meyer Assessment (FMA) and Stroke Upper Limb Capacity Scale (SULCS) were obtained for motor function and activity; Perceptual Threshold of Touch (PTT) and Texture Discrimination Test (TDT) for somatosensory function. Three network indices were created based on standardized individual averaged connectivity values (z-transformed r-values) of predefined regions of interest; interhemispheric, contralesional intrahemispheric, ipsilesional intrahemispheric index. General Linear Models were performed for each network index with time since stroke and mean frame wise displacement as nuisance regressors to determine group differences between stroke patients and healthy controls. Non-parametric partial correlations with the same nuisance regressors were performed to investigate the association between functional connectivity and sensorimotor function.

### Results:

We included four male and five female subacute stroke patients with mean age of 64 years (range: 47-79) and mean time post stroke of 82 days (range: 65-113). Stroke patients showed significant higher functional connectivity compared to healthy controls in ipsilesional ($p=0.001$) and contralesional intrahemispheric index ($p=0.000$). High to moderate correlations were found between higher interhemispheric connectivity index and more impaired clinical somatosensory function ($r=0.85$ for PTT), motor function ($r=-0.44$ for FMA), and motor activity ($r=-0.72$ for SULCS). Moderate correlations were found for more impaired somatosensory function with higher ipsilesional intrahemispheric connectivity for both TDT and PTT ($r=0.42$) and with higher contralesional intrahemispheric connectivity for PTT ($r=0.41$).

### Conclusion:

Stroke patients show increased functional connectivity compared to healthy controls in both hemispheres, and higher functional connectivity between and within both hemispheres is associated with more impaired sensorimotor upper limb function. Our results suggest a negative impact of hyperconnectivity in the non-impaired inter- and intrahemispheric sensorimotor networks of the brain on sensorimotor upper limb function.

## T6: High-functioning Stroke Survivors Require Motor Capabilities Beyond Strength

Neha Lodha, Prakruti Patel
*Colorado State University, Fort Collins, USA*

### Background:

Over 75% of the chronic stroke individuals are high-functioning. Typically, high-functioning individuals experience mild to moderate motor impairments and often resume work or prior activities. This functional independence places high demands on the ability to perform skilled manual tasks and move independently such as walking, and driving. Two potential motor deficits that hinder function in chronic stroke are declines in strength and force control. Here, we quantify impairments in strength and force control and identify their contribution to functional capacity in high-functioning stroke.

### Methods:

High-functioning stroke individuals and age-matched healthy controls participated in this study. High-functioning status was determined with the following criteria: Functional Activity Index (FAI) > 16/45; Fugl Meyer (FM) Lower Extremity Score > 16/32, and FM Upper Extremity Score > 34/66. To examine strength and force control, participants performed the following tasks (1) maximum voluntary contractions (MVC) and (2) visuomotor tracking task. All task were performed with the paretic limb in three contractions: ankle plantarflexion-dorsiflexion, gripping, and finger flexion. Strength was quantified as the maximum force produced. Force control was quantified as (a) the accuracy and (b) variability of force during the visuomotor tracking task. To examine functional capacity, participants performed pegboard dexterity task, steering and braking in simulated driving environment, overground walking. Functional capacity was determined by the time to complete nine-hole-pegboard-test, lane deviation, braking reaction time, and walking speed.

### Results:

High-functioning stroke participants were moderately active (FAI median = 30), had moderate to mild motor impairments (FM median score = 28 for Lower Extremity and Upper Extremity), and showed reasonable grip strength recovery (paretic /non paretic limb = 73.45 ± 22.39%)  Compared with the controls, the high-functioning stroke group demonstrated decreased strength, decreased accuracy, and increased variability of forces (*p*p2 = 0.57, *p*2 = 0.49, *p*2 = 0.22, *p*2 = 0.61, *p*

### Conclusions:

In high-functioning stroke individuals, impaired force control but not strength is a significant contributor of functional capacity in upper (dexterity and steering) and lower limb (braking and walking). Following substantial (> 50%) recovery of strength, any further improvement in functional capacity are more reliant on force control than strength. Rehabilitation interventions that target force control may potentially enhance functional outcomes in high-functioning stroke survivors.

## T7: Promoting Study Power of Stroke Rehabilitation Trials Using a Longitudinal Mixture Model

Rick van der Vliet[1,2], Gert Kwakkel[3,4], Elrozy Andrinopoulou[1], Rinske Nijland[5,3], Maarten Frens[1], Erwin van Wegen[3], Carel Meskers[3], Jorrit Slaman[2], Gerard Ribbers[1,2], Ruud Selles[1]
[1]Erasmus MC, Rotterdam, Netherlands. [2]Rijndam Rehabilitation, Rotterdam, Netherlands. [3]VUmc, Amsterdam, Netherlands. [4]Northwestern Univeristy, Chicago, USA. [5]Reade Rehablitation Center, Amsterdam, Netherlands.

### Objective:
Evidence for effective therapeutic interventions to improve motor recovery post stroke is limited, because the majority of clinical trials lacks are heavily underpowered as a result of the heterogeneity of recovery early post-stroke. The goal of this paper was to compare the power to detect a difference in the Fugl-Meyer assessment of the upper extremity (FM-UE) using the longitudinal mixture model versus a classical statistical model. In addition, we investigated the effect of (1) measurement time and intervention start time noise and (2) follow-up on study power. Finally, we calculated the benefit of patient selection for studies designed to detect an intervention effect in a certain stroke recovery cluster (poor, moderate excellent).

### Methods:
We recently developed a longitudinal mixture model of stroke recovery, identify 3 main FM-UE recovery subgroups. For this study, we amended this longitudinal mixture model of stroke recovery to account for participation in a stroke rehabilitation trial. Using this amended model, we investigated the influence on the power to detect a 4.25 point FM-UE difference of (1) statistical analysis based on this model compared to more classical statistical analysis, (2) timing noise of the measurement, (3) different number of follow-up measurements, and (4) patient selection from a heterogeneous group of primarily patients with poor, moderate of good recovery.

### Results:
To obtain 90% power, the number of patients needed is reduced approximately ninefold from 590 patients for the classical model to 70 patients for the longitudinal mixture model. Measurement time and intervention start time noise do not importantly influence study power in this mixture model approach. A larger number of follow-up measurements, however, increases study power. Patient selection based on the predicted stroke recovery cluster increases the power to detect an intervention effect in a certain cluster, at the cost of falsely excluding patients when the predicted cluster is wrong.

### Interpretation:
The longitudinal mixture model can greatly reduce the number of patients needed to obtain sufficient power and will, therefore, be useful for (1) designing future stroke rehabilitation trials, (2) re-analyzing already completed stroke rehabilitation trials.

## T8: Patient-specific Prediction of Arm-hand Capacity Recovery After Stroke: A dynamic approach

Ruud Selles[1,2], Elrozy Andrinopoulou[1], Rinske Nijland[3], Rick van der Vliet[1], Jorrit Slaman[2], Erwin van Weegen[4], Carel Meskers[4], Dimitris Rizopoulos[1], Gerard Ribbers[1,2], Gert Kwakkel[4]

*[1]Erasmus MC, Rotterdam, Netherlands. [2]Rijndam, Rotterdam, Netherlands. [3]Reade Rehabilitation Center, Amsterdam, Netherlands. [4]Amsterdam UMC, Location VU University Medical Center, Amsterdam, Netherlands.*

### Introduction:

Prediction of upper limb recovery after stroke is an important aspect of expert care. At present, the majority of stroke recovery prediction models use classic regression modeling. Limitations of these models include that the prediction accuracy strongly depends on the timing of fixed baseline and follow-up measurements and that these models only predict the outcome at one specific moment or outcome. To overcome these limitations, we introduce a mixed-effects model for a prediction of stroke recovery that incorporates all available information of patients. Specifically, we predict upper extremity capacity measured using the Action Research Arm Test (ARAT) score can be updated each time new information becomes available (‘dynamic prediction’).

### Methods:

We combined data on upper extremity capacity recovery in first-ever ischemic anterior circulation stroke patients from four early post-stroke prospective cohort studies with repeated measurements in time. Upper extremity capacity was measured with the Action Research Arm Test (ARAT) and we included a large number of potential covariates.
We developed a mixed-effects model allowing an unequal number of follow-up measurements between subjects, a non-linear time course and varying time points of the repeated measurements. A first online environment of these predictions is available at https://emcbiostatistics.shinyapps.io/DynamicPredictionARATapp/. To establish the prediction accuracy of the different models, we performed a 5-fold cross-validation procedure.

### Results:

The data set consisted of 450 patients. Comparing different potential mixed-effects models, we found that a model with only the significant covariates and the significant interactions with time was almost as good as more complex models. Because of this, we decided to further continue with this more simple model. The cross-validation indicated that the prediction errors at 6 months post-stroke decrease as the number of measurements used for modeling increase, from a median error when one measurement was used of 9.7 points on the ARAT (Q1-Q3: 1.0-30.3) to 1.03 (Q1-Q3: 0-4.3) when seven measurements were used for modeling. The prediction model was real-time coupled to a data acquisition environment to allow real-time prediction for individual patients.

### Discussion:

We introduce a mixed-model approach to predicting stroke recovery. Important advantages compared to classical prediction models include that 1) all available repeatedly-measured information from a subject can be included to predict the outcome, 2) a recovery time-course is predicted instead of a single future time-point, 3) the prediction can be updated each time new information becomes available (‘dynamic prediction’) 4) exact time moments are used to predict outcome, and 5) the predictions can be obtained real-time in a system coupled to a data acquisition environment. Median 6-month prediction errors reduce from 9 ARAT points early post-stroke to 1 ARAT point several weeks later.

## T9: Ipsilateral Corticomotor Control of the Paretic Limb During Bilateral Ankle Movement After Stroke

Brice Cleland, Sangeetha Madhavan
*University of Illinois at Chicago, Chicago, USA*

### Introduction:
Increased ipsilateral motor control of the paretic limb by the contralesional hemisphere may contribute to walking impairment after stroke. Ipsilateral motor evoked potentials (MEPs) in the paretic lower limb following transcranial magnetic stimulation (TMS) are associated with slower walking speeds and more structural damage to the ipsilesional corticospinal tract. Most studies have evaluated ipsilateral motor control of the paretic limb in the upper limb and during isometric tasks. No studies have evaluated this construct during dynamic lower limb tasks, which is necessary to translate these findings to walking rehabilitation. Thus, this study evaluated ipsilateral motor control of the paretic limb during dynamic, bilateral ankle contractions. We hypothesized that ipsilateral motor control would be greater in the paretic vs. the non-paretic limb and greater during dynamic vs. isometric ankle contractions.

### Methods:
In this ongoing study, ten individuals with chronic stroke (60±5 years, 2 female) performed dynamic, bilateral reciprocal ankle dorsiflexion and plantarflexion. At peak muscle activity in the tibialis anterior (TA) of the target limb, TMS was applied to the ipsilateral or contralateral hemisphere. Twenty stimuli at 120% of active motor threshold were applied to each hemisphere for each target leg. TMS was also applied during dynamic, unilateral ankle movement and during isometric, unilateral contractions at the same percentage of maximal electromyography (EMG) signal as during dynamic ankle movements. MEP amplitude was assessed as the area of the rectified MEP normalized to background EMG. The degree of ipsilateral motor control of the target limb was assessed as a ratio of MEP amplitudes: .

### Results:
Preliminary results show that during dynamic, bilateral ankle movement, ipsilateral motor control tended to be greater in the paretic (ratio=0.11) than in the non-paretic limb (ratio=0.25; $p$=0.21). In contrast, there was minimal difference between limbs during isometric, unilateral ankle contractions (paretic ratio=0.20, non-paretic ratio=0.24; $p$=0.67). Ipsilateral motor control tended to be greater during dynamic than isometric ankle contractions in the paretic limb ($p$=0.17) but not in the non-paretic limb ($p$=0.92). Data from dynamic, unilateral ankle contractions were similar to those during dynamic, bilateral ankle contractions.

### Discussion:
Results support our hypotheses that ipsilateral motor control is greater in the paretic than the non-paretic limb and greater during dynamic than isometric contractions. Similarities between unilateral and bilateral dynamic ankle movements suggest that the degree of ipsilateral motor control is influenced by whether the task is isometric vs. dynamic, not unilateral vs. bilateral. Our results suggest that ipsilateral motor control should be measured during tasks involving dynamic movement to provide insight about functional lower limb movements. Our results also provide insight into how neuromodulatory adjuvants can be used to enhance walking rehabilitation.

T10: Exploring the Use of Visuospatial Tests to Predict Motor Learning Capacity in Older Adults

Jennapher Lingo VanGilder[1], Kevin Duff[2], Keith Lohse[3], Kyle Elliott[1], Peiyuan Wang[1], Sydney Schaefer[1,3]
*[1]Arizona State University, Tempe, USA. [2]University of Utah Hospital, Salt Lake City, USA. [3]University of Utah, Salt Lake City, USA*

Background:
Age-related declines in motor learning may be related to declines in visuospatial function, regardless of baseline motor function or other cognitive impairments. Thus, visuospatial tests may be useful for evaluating older patients' motor learning capacity prior to therapy. The purpose of this study was to identify which visuospatial test is most predictive of motor learning within an older cohort.

Methods:
Thirty-two participants (mean±SD age=70.5±6.7) with no self-reported neurological damage completed six visuospatial tests of perception (Line Orientation), construction (Rey-Osterrieth Complex Figure Copy and Block Design), memory (Rey-Osterrieth Complex Figure Recall), attention (Visual Puzzles), and abstraction (Matrix Reasoning). Participants then completed three weekly training sessions on a functional upper-extremity motor task (i.e., task-specific training), and were re-tested one month later on the trained task and another untrained upper-extremity motor task to evaluate the durability and generalizability of motor learning, respectively. Performance on both motor tasks was measured as movement time, with lower values indicating better performance. Principal component analysis was used to reduce the dimensions of the visuospatial battery for inclusion in a regression model; principal components (PCs) with Eigenvalues > 1.00 were included. A mixed-effects model assessed one-month follow-up performance as a function of baseline performance and the PCs from the visuospatial battery.

Results:
Factor analysis indicated the visuospatial tests loaded on two PCs with Eigenvalues > 1.00. Block Design and Matrix Reasoning loaded most heavily on PC1 ($r>0.78$), whereas Figure Copy and Figure Recall loaded most heavily on PC2 ($r>0.73$). Both PCs were included as predictors in the mixed-effects model. For the trained task, participants improved by a mean of 23.8% (14.7 seconds) from baseline to one-month follow-up ($Z=-261$, $p<0.0001$), with follow-up being positively related to baseline performance ($\beta=0.50$, $p<0.0001$), but not PC1 ($\beta=0.02$, $p=0.96$), nor PC2 ($\beta=0.84$, $p=0.22$). Similarly, participants significantly improved on the untrained task from baseline to one-month follow-up by 14.7% (6.6 seconds), despite no training ($Z=-110$, $p<0.018$), with follow-up being positively related to baseline performance ($\beta=0.50$, $p<0.001$) and unrelated to PC1 ($\beta=-0.10$, $p=0.80$). Follow-up on the untrained task was, however, positively related to PC2 ($\beta=1.47$, $p=0.024$). Because our previous studies were unable to disentangle visuospatial from executive function, we ran a second PCA to include an executive function measure (Coding). Coding loaded on PC1 ($r=0.54$) and the mixed-effects model results remained unchanged (i.e., PC1 remained unrelated to the durability nor generalizability of learning).

Discussion:
Motor learning capacity may be evaluated using the Rey-Osterrieth test, which could be administered prior to motor training and may relate to risk of non-responsiveness in therapy. Results also suggest neural pathways underlying visuospatial construction and memory are necessary for the generalizability of motor learning, rather than its durability in response to extensive training.

## T11: The Effect of Myoelectric Computer Interface Training on Arm Kinematics and Function After Stroke

Siva Nalabothu[1,2], Ishaar Ganesan[1,2], Torin Kovach[1,2], Marc Slutzky[2]
*[1]Illinois Mathematics and Science Academy, Aurora, USA. [2]Northwestern Feinberg School of Medicine, Chicago, USA*

First reported in the 1900s, irregular muscle coactivation is prevalent in many stroke cases, and a rehabilitation method for this muscle coactivation is imperative. A new technology overcoming motor-based impairments faced by stroke survivors, brain-neural computer interaction systems connect the external world to the brain via electoral and other biosignals in a manner that engenders extreme restorations of motor functions. The Myoelectric Computer Interface (MCI) is a pertinent system that uses electromyographic signals attached to the muscle to communicate with a computer and project programmable visual-auditory representation feedback of the irregular coactivation of muscles. Tomic et al. initially designed a paradigm utilizing a game controlled by the MCI to be conducive to the reduction of abnormal coactivation of muscles in stroke survivors. Resulting in improvements in arm function, strength, and range of motion in participants, the MCI proved successful in the Tomic et al. study. However, this MCI training only allowed for responses and recordings of a singular pair of arm muscles, leading to the patients having to switch many times between each muscle pair during their training program. As brain-machine interfaces and brain-neural interaction systems implementing more than two muscles or biosignals have been shown to be effective in refining motor control and kinematics, we have redesigned the MCI to implement not only three electromyography (EMG) signals from three different muscles at once but also a sham paradigm to act as a control group. Our method of conveying feedback to the stroke patients is a three-dimensional game comprising an X, Y, and Z axis, with each muscle controlling its respective dimension. By comparing this novel system to the previous training over a six week period, we have evaluated the effects of MCI training on coactivation, arm kinematics, and motor function in patients exhibiting abnormal muscle coactivation. The original paradigm has been effective in reducing muscle coactivation, the sham paradigm has not been effective in reducing muscle coactivation, and the three-muscle paradigm has been significantly more effective in reducing muscle coactivation than the original paradigm.

## T12: Using Motor Behavior to Predict One-Year Declines in Activities of Daily Living in Older Adults with Amnestic Mild Cognitive Impairment

Sydney Schaefer[1,2], Kayla Suhrie[2], Kevin Duff[2]
*[1]Arizona State University, Tempe, USA. [2]University of Utah, Salt Lake City, USA*

Changes in activities of daily living (ADLs) over time are important to monitor in older adults at risk for dementia, such as those with amnestic Mild Cognitive Impairment, a prodrome to Alzheimer's disease. Sharp declines in ADLs can indicate disease progression and symptom worsening. Current methods for predicting such declines (e.g., brain amyloid imaging, cognitive performance) poorly correlate with these declines. We have recently developed a brief, low-cost upper extremity motor task that is easy to administer to older adults and correlates with cognitive function. Thus, the purpose of this study was to determine the extent to which this motor task could predict changes in ADL function over one year. Eighty-two adults diagnosed with amnestic Mild Cognitive Impairment (mean±SD age: 75.5±5.9 years) completed the motor task using their dominant hand, which involved transporting raw kidney beans from one of four small cups as quickly as possible (see Schaefer 2015). They also completed the following ADL measures: the Alzheimer's Disease Cooperative Study-Activities of Daily Living for Mild Cognitive Impairment (ADCS-ADL-MCI) Scale and three of the five subtests of the Independent Living Scale (ILS): Health & Safety, Managing Money, and Managing Home and Transportation. The ADCS-ADL-MCI scale assesses self- and informant-reported functional capacity across basic and complex ADLs in individuals with MCI. The ILS assesses competency in instrumented activities of daily living through direct observation (rather than self-report) and is reported as standard scores. Participants completed these ADL measures during the same session as the motor task, and again one year later (mean±SD: 1.32±0.13 years). All measures except for the ILS Managing Money subtest showed significant decline over the one-year period, as determined by 95% CI. Multiple linear regression indicated that motor task performance (measured in seconds) was a significant predictor of the amount of decline across the self-reported ADCS-ADL scale ($p=.038$) and the ILS Health & Safety subtest ($p=.003$), such that slower times on the motor task were associated with more decline in ADL function over the following year, even after accounting for differences in baseline ADL function. No predictive relationship was observed for the informant-reported ADCS-ADL scale ($p=.12$) or the ILS Managing Home and Transportation ($p=.36$). These results suggest that differences in motor behavior among older adults may reflect different trajectories of functional decline, and may have clinical utility in the earlier identification of dementia risk.

T13: Five Simple Rules to Assessing Clinical Literature: A perspective for the practicing clinician in stroke rehabilitation

Jonathan Tsay[1], Carolee Winstein[2]
*[1]University of California Berkeley, Berkeley, USA. [2]University of Southern California, Los Angeles, USA*

Neurorehabilitation relies on core principles of neuroplasticity to awake latent neural connections, promote detour circuits, grow new synapses and neurons, and reverse impairments. Clinical interventions grounded in these principles have been shown to promote recovery, while demoting compensation. However, many clinicians struggle to find evidence from our growing but nascent body of literature to efficiently implement these principles in their practice. Regulatory bodies and organizational balance sheets further discourage methodical, time-intensive, and efficacious clinical interventions because the lure of more immediate functional success is so great. Modern neurorehabilitation practice that results from these pressures favors strategies that encourage compensation over those that promote recovery (Kitago et al., 2013). The tension between practical and scientific drivers of neurorehabilitation practice frustrates even the best clinicians (Ofri, New York Times June 8, 2019, Opinion Piece; Cramer et al., 2017). Recent work provides evidence that recovery-promoting practices can be effective and durable, even in chronic stroke survivors (Ward et al., 2019). This successful program was 3 weeks in length, administered in an outpatient setting, and lasted up to 6 hours per day. Every 90 min private session was progressed and tailored to the individual patient.

With a focus on guiding the busy clinician through the rapidly growing clinical literature for compelling evidence that supports recovery, we provide a set of 5 simple rules that can be used to evaluate the pre-clinical/ early-stage clinical trials (Dobkin 2009):

Rule 1: Principles of neuroplasticity motivated the intervention

Rule 2: Clinical impairment scales and measures of motor control were used to assess recovery

Rule 3: Bench knowledge was appropriately applied to the bedside.

Rule 4: Converging lines of evidence supported the study's conclusion(s).

Rule 5: Meaningful and individualized tasks were chosen to engage the stroke survivor.

These rules point clinicians toward literature that values the biological recovery process over the more alluring functional recovery mantra. Filtering the literature through this critical lens will foster new clinical research inspired by improved outcomes (e.g. Wade et al., 2019). Each rule is motivated with examples from the literature and designed to promote a culture which values brain recovery over compensation in the clinic. This perspective is meant to serve a new generation of scientifically-minded clinicians, students, and trainees poised to not only meaningfully advance our field but to also erect policy changes for better stroke care.

## T14: On the Importance of Gait Speed: Perspectives from people with multiple sclerosis and neurologic physical therapists

Prudence Plummer, Andrea Stewart, Jessica Anderson
*University of North Carolina, Chapel Hill, USA*

### Background:

It is not clear whether gait speed, the most widely-used measure of treatment efficacy for gait impairment in MS, is an important aspect of mobility for patients.

### Objective:

To identify the aspects of mobility that are most important to people living with MS and physical therapy clinicians, and to gain insight into how patients and clinicians perceive whether physical therapy has been effective.

### Methods:

46 people with MS and 23 physical therapists participated in either a focus group, an interview, or an electronic survey. Participants with MS were asked to identify the types of walking difficulties they experience and to describe their goals, expectations, and satisfaction with prior physical therapy. Physical therapy clinicians were also asked to identify mobility-related problems in people with MS and to describe the treatment activities and outcome measures to document effects of treatment. Both people with MS and clinicians were asked specifically about the importance of walking speed and how they decide if physical therapy has been effective.

### Results:

Among people with MS, the two most important aspects of mobility disability were falls and difficulties getting out into the community. Other important aspects of mobility for people with MS were fatigue, foot drop and other lower extremity weakness, and impaired sensation. Walking speed was infrequently described as a problem by people with MS. Therapists also identified falls and safety as most important. Walking speed is often measured by clinicians but rarely a goal of treatment. Although safety was of prime importance to clinicians, they lacked certainty about their ability to objectively measure improvements in safety. People with MS evaluated physical therapy effectiveness based on the ease by which they can do things. They also acknowledged that “not getting worse” is a positive outcome. Therapists assess effectiveness based on amount of change in objective outcome measures, and by patient and caregiver reports of improved function.

### Conclusions:

Gait speed is not of major importance to people with MS or physical therapy clinicians. People with MS want to be able to walk further and without an assistive device, and they want to avoid falls. Therapists want to maximize safety while improving functional ability. These findings are incongruent with numerous pharmacological and rehabilitation clinical studies in which gait speed is the primary efficacy endpoint.

## T15: Deep Brain Stimulation of the dendatothalamocortical pathway modulates motor cortical rhythms in stroke patients

***Fletcher H. McDowell Award Finalist**

Raghavan Gopalakrishnan[1], Kenneth Baker[2], David Cunningham[3], Nicole Mathews[2], Brett Campbell[2], Alexandria Wyant[4], Andre Machado[1,5]

*[1]Center for Neurological Restoration, Cleveland Clinic, Cleveland, USA. [2]Neurosciences, Cleveland Clinic, Cleveland, USA. [3]Physical Medicine and Rehabilitation, Case Western Reserve University, Cleveland, USA. [4]Biomedical Engineering, Cleveland Clinic, Cleveland, USA. [5]Neurosurgery, Cleveland Clinic, Cleveland, USA*

### Introduction:

Stroke is a leading cause of long-term disability in the United States and the industrialized world. Despite progress in acute interventional strategies aimed at protecting tissue and reducing infarct volume, relatively few efforts have been made to enhance plasticity and recovery of function in the chronic phase after stroke. We are currently investigating deep brain stimulation of the dentatothalamocortical pathway (DN-DBS) in stroke patients that exploits the natural neural pathways via thalamocortical connections to promote cortical activity and excitability in the perilesional cortex (Machado et al, 2013).

In this project, we examined the acute effects of DN-DBS on cortical excitability using electroencephalography (EEG) during the execution of a motor task. Our goal was to identify specific DN-DBS contacts and parameters that facilitate motor behavior that could eventually inform therapeutic programming. We adopted Event-related desynchronization/synchronization (ERD/ERS) analysis, a well-established model to investigate the movement related modulation of EEG rhythms in the alpha (8-12 Hz) and beta (13-30 Hz) bands over the premotor and sensorimotor cortex (Pfurtscheller et al., 1996). Recent research has found the amplitude of ERS to be an indicator of percentage effort and rate of force exerted during the execution of motor tasks (Fry et al. 2016). Hence, we specifically investigated the modulation of ERS over the perilesional cortex by DN-DBS. We hypothesized that DBS induced reduction in ERS amplitude could be a surrogate marker of facilitation of task effort and hence cortical excitability.

### Methods:

Patient's performed a visually cued grip task using a dynamometer while EEG was acquired continuously. The visual cues indicated the onset of a preparatory phase, a contraction phase, and a relaxation phase. Patients were instructed to squeeze the dynamometer during the contraction phase to vertically move a ball (on a computer screen) from baseline to a predetermined target level, and then relax upon successfully completing the task. The task was performed on an average of 70 trials, for both DBS OFF and ON conditions. The percentage effort during the task was set to ~20% maximal voluntary force elicited by the patients during the OFF condition, and was kept constant between DBS OFF and ON conditions.

### Results:

Stroke patients exhibited greater ERS amplitude indicative of increased effort on the affected extremity during the task. We found that only select DBS parameter configuration (contact location, current and pulse width) significantly attenuated the ERS amplitude. These were identified as potential settings that could be used for therapeutic programming.

### Conclusion:

The results show that ERS could be a potential marker of cortical excitability that could be complementary to motor behavioral metrics to determine therapeutic effects of DBS. Future work will correlate task behavior and ERS modulation to further substantiate the observed findings.

T16: Kinematic Measures of Ipsilesional Arm Motor Performance Significantly Predict Both Functional Movement Deficits and Overall Functional Independence in Moderate-to-Severely Impaired Chronic Stroke Survivors

Shanie Jayasinghe[1], Candice Maenza[1], David Good[1], Carolee Winstein[2], Robert Sainburg[3]
*[1]Penn State College of Medicine, Hershey, USA. [2]University of Southern California, Los Angeles, USA. [3]The Pennsylvania State University, University Park, USA*

Our previous research has indicated that ipsilesional arm motor deficits tend to be most extensive in patients with severe contralesional paresis. Because these patients are unable to use the paretic arm for functional manipulation, ipsilesional arm movement deficits are likely to impair both functional motor performance and overall functional independence in this population. We tested this hypothesis by examining the relationship of kinematic measures of motor performance (i.e. high-resolution, continuous) in the ipsilesional arm with clinical measures of motor performance (i.e. low-resolution, discontinuous). We also measured the kinematic quality of motor performance in the paretic arm and assessed potential relationships between movement quality in the contralesional and ipsilesional arms.

Our preliminary findings include data from 11 chronic stroke survivors with unilateral stroke lesions (3 right hemisphere deficits; 2 females). Our clinical measures include the upper extremity portion of the Fugl-Meyer motor assessment (UEFM) for the contralesional arm and the Jebsen Taylor Hand Function Test (JTHFT) for the ipsilesional arm. Overall functional independence was measured using both the Barthel index (BI) and the self-care portion of the Functional Independence Measure (FIM). High resolution arm kinematics were obtained during horizontal plane tasks performed on the KineReach virtual reality system, with the arms supported on air sleds to reduce the effects of gravity and friction. For the contralesional arm, participants circumscribed the largest area possible on the work surface. Ipsilesional arm performance was tested during a planar 3-target reaching task, for which we quantified movement time, initial direction error, final position error, and linearity.

Not surprisingly, we confirmed a relationship between paresis and functional independence: higher scores on the UEFM corresponded to higher scores on the FIM ($r=0.6$). More surprisingly, our results indicate a strong relationship between ipsilesional movement kinematics and both functional performance and overall functional independence: movement linearity was strongly correlated with the BI ($r=-0.6$) and the JTHFT without writing ($r=0.7$), movement time was correlated with the JTHFT without writing ($r=0.58$), while initial direction error correlated ($r < -0.7$) with both measures of functional independence (BI, FIM). For the paretic arm, our kinematic measure of work area correlated strongly ($r>0.6$) with specific components of the UEFM (proprioception, wrist & hand score). We also found a significant correlation ($r=-0.48$) between work area and initial direction error in the ipsilesional arm.

These findings support the hypothesis that ipsilesional arm impairments limit functional performance and independence in patients with severe contralesional paresis. Our findings also indicate that, even within this restricted group of patients, kinematic measures of contralesional arm impairment significantly predict kinematic deficits in the ipsilesional arm, a finding consistent with our bihemispheric model of motor control.

T17: Handedness, Rather Than Injury Side or Severity, Determines Hand Choices After Unilateral Injury

Madeline Thompson, Maureen Hyde, Susan Mackinnon, Benjamin Philip
*Washington University School of Medicine, St. Louis, USA*

Unilateral sensorimotor impairment occurs after a variety of insults to the central and peripheral nervous system, but few studies have addressed how unilateral-specific factors (i.e. handedness) impact post-injury action and participation. Here, we addressed this via a single-arm observational study of 48 adults with unilateral upper extremity peripheral nerve injury. We hypothesized that an injury to the dominant hand would have a greater impact on hand usage (left/right choices) and life-relevant factors (e.g. quality of life) than injury to the non-dominant hand. We also explored our data to identify relationships between 10 measures of capacity (laboratory performance), 4 of hand usage and 4 life-relevant factors. We confirmed an effect of injury side (dominant vs. non-dominant) on hand usage, but not quality of life. Specifically, participants continued to use their dominant hand regardless of whether it was the injured hand. This held true across a wide range of peripheral nerve injury severity, except for the most severe impairments. In our exploratory analysis, multiple linear regressions revealed only one measure of capacity associated with a life-relevant factor: tactile sensory threshold loss on the fingertip, which contributed to a model of health-related quality of life. Because standard measures of life-relevant factors may be insensitive to unilateral impairment, we performed a post-hoc analysis of unilateral activities, and found that participants with dominant hand impairment were more likely (vs. patients with non-dominant hand) to decrease use of their injured arm to turn a key or write. We conclude that clinicians should expect clients with unilateral impairment to continue using their dominant hand regardless of injury side, except for the most severe impairments; and that clinicians can learn about quality of life by assessing tactile sensory loss in the fingertips. However, relationships between capacity and participation remain elusive in these patients, in part because current measures of participation are not designed to identify the specific consequences of unilateral impairment.

## T18: Predicting Upper Limb Recovery After Stroke Following the Extended Proportional Recovery Rule

Rick van der Vliet[1], Ruud Selles[1], Carel Meskers[2], Gert Kwakkel[2]
[1]*Departments of (1) Neuroscience, (2) Rehabilitation Medicine and (3) Plastic and Reconstructive Surgery, Erasmus Medical Center, Rotterdam, Netherlands.* [2]*Department of Rehabilitation Medicine, Amsterdam University Medical Centre, location VU University Medical Center, Amsterdam Neurosciences and Amsterdam Movement Sciences, Amsterdam, Netherlands*

### Objective:

Spontaneous recovery is an important determinant of upper extremity recovery after stroke, and has been described by the 70% proportional recovery rule for the Fugl-Meyer motor upper extremity (FM-UE) scale. However, this rule is criticized for overestimating the predictability of FM-UE recovery. Our objectives were to (1) develop a longitudinal mixture model of stroke recovery, (2) identify FM-UE recovery subgroups, and (3) cross-validate the model predictions.

### Methods:

We developed an exponential recovery function with the following parameters: subgroup assignment probability, proportional recovery coefficient , time constant in weeks , and distribution of the initial FM-UE scores. We fitted the model to FM-UE measurements of 385 first-ever ischemic hemispheric stroke patients and cross-validated the endpoint predictions and cluster assignment.

### Results:

The model distinguished five subgroups with different recovery parameters (r1=0.09; tau1=5.2; r2=0.47; tau2= 0.6; r3=0.87; tau3=9.9; r4=9.9; tau4=2.6; r5=0.93; tau5=1.2). Endpoint FM-UE was predicted with a median absolute error of 5.4 IQR=[1.4-12.9] at 1 week post stroke and 4.4 IQR=[1.4-10.0] at 2 weeks. Overall accuracy of assignment to the poor (subgroup 1), moderate (subgroups 2 and 3) and excellent (subgroups 4 and 5) recovery clusters was 0.78 95%ETI=[0.77-0.80] at 1 week post stroke and 0.80 95%ETI=[0.79-0.81] at 2 weeks.

### Interpretation:

FM-UE recovery reflects different subgroups, each with its own recovery profile. Cross-validation indicates that FM-UE endpoints and cluster assignment can be well predicted. These findings will have major implications for the identification of prognostic biomarkers and designing stroke recovery and rehabilitation trials.

T19: Effects of Physical Activity Interventions on Primary Motor Cortex BOLD Profile in Unimanual Movements

Javier Omar[1], Lisa Krishnamurthy[2,3], Kevin Mammino[2], Bruce Crosson[2,1,3], Giri Krishnamurthy[2,1], Joe Nocera[2,1], Keith McGregor[2,1]
*[1]Emory University, Dectur, USA. [2]Atlanta VA Medical Center, Decatur, USA. [3]Georgia State University, Atlanta, USA.*

The current study aimed to examine the impact of a 12-week aerobic exercise intervention on relateralizing motor function to a single hemisphere in sedentary older adults. Twenty-four participants were randomized into an aerobic, spin cycling exercise group or a non-aerobic balance training group. Participants completed a pre- and post-intervention battery of motor control tasks and a pre- and post-intervention cardiovascular fitness assessment (estimated VO2max). Magnetic resonance images were acquired prior to and after the intervention and a block-design, right-hand motor task was used to evaluate interhemispheric cortical activation patterns. The aerobic exercise group showed significant improvements in their cardiovascular fitness as compared to the balance group. A significant decrease in bilateral primary motor cortex (M1) activity was not observed between the aerobic exercise group and the balance group. It was observed that those who completed the aerobic exercise intervention showed less left M1 and supplementary motor area (SMA) activity as compared to who that completed the non-aerobic, balance intervention. Significant differences in motor performance were not observed between the groups although there was a trend for improved motor performance for those in the aerobic exercise condition as compared to those in the balance condition. In conclusion, the current study provides preliminary evidence that a 12-week aerobic exercise intervention has the potential to alter cortical activation patterns. The present work also provides evidence suggesting that these changes in cortical activation patters may be associated with clinically relevant improvements in motor functioning.

## T20: Elucidating the Role of Contralesional Motor Cortices in Upper Limb Functional Motor Recovery after Stroke

Ela Plow[1], Yin-Liang Lin[2], Vishwanath Sankarasubramanian[3], Kelsey Potter-Baker[4], David Cunningham[5], Kyle O'Laughlin[1], Adriana Conforto[6], Ken Sakaie[1], Xiaofeng Wang[1], Jayme Knutson[5], Andre Machado[1]
*[1]Cleveland Clinic Foundation, Cleveland, USA. [2]Dept. of Physical Therapy and Assistive Technol., Natl. Yang-Ming Univ., Taipei, Taiwan. [3]University of Michigan, Ann Arbor, USA. [4]University of Texas, Rio Grande Valley, USA. [5]MetroHealth, Cleveland, USA. [6]University of Sao Paulo, Sao Paulo, Brazil.*

The role of contralesional motor cortices in chronic upper limb motor recovery following stroke remains unclear. Classical evidence suggests that contralesional role is *negative*, that these regions impose excessive inter-hemispheric inhibition (IHI) on ipsilesional regions to limit motor output. More recent evidence suggests that contralesional role may be *positive*, that these areas may contribute to paretic limb movement in patients lacking sufficient ipsilesional resources. A new model - the 'bimodal-balance recovery hypothesis'(Di Pino et al. *Nat Rev Neurol* 2014) suggests that the nature of contralesional influence may vary based on the severity of corticospinal injury/impairment, being *negative* in the presence of minimal injury/impairment, and *positive* in the presence of severe injury/deficit. This hypothesis, however, remains to be validated, and criterion severity level stratifying patients with differing contralesional influences is yet to be identified. Resulting knowledge will be valuable for developing severity-specific treatments. We performed two studies. Study 1 characterized how contralesional role varies across the range of corticospinal injury and motor impairment, and identified the criterion severity level stratifying patients with differing contralesional roles. Study 2 evaluated how stratified patients respond to excitation or suppression of contralesional cortices achieved with brain stimulation. Twenty-five patients with a wide range of upper extremity motor impairment participated in study 1 and another 24 participated in study 2 (chronic, >6mths). Transcranial Magnetic Stimulation (TMS) was used to measure IHI from contralesional motor cortices and residual corticospinal excitability. Diffusion Tensor Imaging (DTI) was used to assess the extent of corticospinal injury. In study 2, patients received repetitive TMS (rTMS), 1-Hz for suppression and 5-Hz for excitation of contralesional motor cortices given for single session each in a crossover, sham-controlled design. Motor improvement was measured as reduction in reaching response time. Study 1 revealed a parabolic relationship between IHI and motor impairment (Fugl-Meyer, FM, best =66). In patients with FM >43, IHI was stronger with lower FM, while in patients with FM <43, IHI was weaker with lower FM. This suggests that the nature of contralesional influence is more inhibitory in moderate/mildly-impaired patients and less inhibitory in the more severely impaired- a finding that aligns with the new bimodal-balance recovery hypothesis. FM 43 (confidence interval 40-46) may be a useful biomarker to stratify patients with differing contralesional influences. Study 2 provided initial validation for this criterion. Patients with FM >43 responded to contralesional suppression via gain in residual corticospinal excitability, which implies contralesional motor cortices have an *inhibitory* influence on movement in this moderate/mildly-impaired sub-group. Patients with FM <43 responded to contralesional excitation via further reduction in IHI, which implies that contralesional motor cortices have a *positive* influence on movement in this severely impaired sub-group. Our findings have implications for design of precise, effective treatments.

## T21: The Effects of Heel Lifts on Dynamic Measures of Gait and Static Posture and In Individuals with Parkinson's Disease

Liz Jusko, Breanna Roderos, Sarah Uno, Jennifer Hastings
*University of Puget Sound, Tacoma, USA*

### Objective:

The purpose of this study is to determine if step length, gait speed, overall Time Up and Go (TUG) scores, postural alignment, perceived stability, and balance confidence improve with the use of accommodating heel lifts in people with Parkinson's disease (PD).

### Background:

Hastings et al (2018) addressed postural instability in PD subjects with in-shoe heel lifts, finding heel lifts significantly increased upright postural alignment and perceived stability, and that the Falls Efficacy Scale correlated to the amount of dorsiflexion one lacked.

### Design/Methods:

This is a longitudinal, repeated measures study following up on the study by Hastings et al. A convenience sample was obtained from individuals within the local community that were diagnosed with PD. The study received Institutional Review Board approval, and informed consent was obtained from all participants prior to their participation. 18 participants with PD who could independently ambulate 30 feet with or without an assistive device, and able to sit and stand from a chair without assistance, were provided heel lifts based on the severity of their PF contractures. Those with less than 5 degrees of PF contracture were assigned a heel lift of 0.5 cm, and those with a PF contracture between 5-9 degrees were assigned a heel lift of 0.9 cm. One participant was excluded due to incorrect use of the heel lift. Outcome measures taken with and without the heel lifts in place, at two data collection dates, including the activities-specific balance confidence (ABC) scale for balance confidence, postural alignment measurements from the sagittal view photograph, numeric analog scale for perceived stability, the TUG test, and video analysis of TUG trials. The ABC scale was collected at baseline and after two weeks of heel lift use, otherwise outcome measures were performed in the reverse order on the first and second session to account for ordering, practice, and fatigue effects. Participants were instructed to keep the heel lifts inside of their shoes for the two week period between testing sessions. In addition to this, each participant kept a log for the tracking of use of heel lifts.

### Results:

Paired t-tests for outcome measures showed significance in improved postural alignment, but no significance difference in perceived stability, or balance confidence with the use of the heel lifts. No gait measurements showed significant change. Pearson product correlation revealed no correlation between the degree of PF contracture and ABC scale.

### Conclusion:

From this study, we show that accommodating PF contractures with heel lifts significantly improves postural alignment, but has no significant effect on step length, gait speed, or overall TUG score in individuals with PD.

T22: Through Thick and Thin: How sparing of the spinal cord after injury influences motor recovery

Aaron Carrillo, Kelsey Baker
*University of Texas Rio Grande Valley, Edinburg, USA*

Introduction:

A spinal cord injury (SCI) to the cervical spine, can result in varying degrees of damage to the spinal cord. Animal models have suggested that the amount of sparing to neuronal tissue in the spinal cord after SCI can greatly influence baseline function and motor recovery potential. Translating such findings from animal studies to human studies in chronic SCI has been challenging due to a lack of neuroimaging software capable of accommodating metal artifacts or SCI-related edema. Here, we report our findings using a recently released open-source software capable of assessing neuronal sparing in the spinal cord in the presence of such impediments. Specifically, we evaluated how changes in neuronal sparing in the spinal cord in patients with chronic SCI influenced baseline motor function and therapeutic recovery potential.

Methods:

T2-weighted images were collected and analyzed to observe the spinal cord in eight patients with an SCI and healthy controls. Spinal Cord Toolbox was used to map and digitally straighten the spinal cords. Straightening the spinal cords of each patient allowed for a uniform and accurate assessment at each level of the spine to be used across all patients and healthy subjects. Using the output of the software, we labeled each of the vertebrae and determined the cross-sectional area (CSA). CSA was used as a metric of neuronal sparing and was defined as a value in $mm^2$. The CSA of the spinal cord was then analyzed at the site of, rostral, and caudal to the injury. We then determined the relationship between the spinal cord CSA, muscle strength and therapy efficacy using regression analysis. All statistical analysis was performed using SPSS.

Results:

The average spinal cord cross sectional area of healthy controls were found to be 92.43 $mm^2$. In contrast, SCI patients displayed an average of 52.86 $mm^2$, a substantial 42.81% loss of matter rostral, caudal and within the site of injury. We found a 50.56% loss of white matter at the site of the injury, 42.83% rostral to the injury, and 36.51% caudal to the injury when compared to healthy controls. Interestingly, the greatest loss of matter occurred immediately caudal to the epicenter of the injury. Regression analysis suggested that patients with more residual neurons post-injury recovered more upper extremity motor strength following two weeks of rehabilitation (R=0.666). Increased neuronal sparing also suggested greater recovery potential for dexterity(R=0.711) and proximal muscle strength (R=0.292).

Conclusions:

Our results suggest that spinal cord cross-sectional area may serve as an ideal biomarker to determine the recovery potential of any patient with an SCI.T herefore, our findings encourage further studies to examine the role white matter degeneration on the value of current treatment pathways for patients suffering from debilitative spinal cord injuries.

## T23: Performance Differences Between Electroencephalography and Electromyography Biofeedback Training in Stroke Rehabilitation

Octavio Marin-Pardo, Athanasios Vourvopoulos, Meghan Neureither, David Saldana, Esther Jahng, Sook-Lei Liew
*University of Southern California, Los Angeles, USA*

Biofeedback (BF) of electrical activity from brain and muscles, using electroencephalography (EEG) and electromyography (EMG), has been shown to encourage recovery of brain-to-muscle pathways following stroke. However, previous studies have found conflicting evidence of these methods for recovery in patients with varying degrees of voluntary movement. It is unclear whether EEG, EMG or a combination of both can facilitate motor recovery and, if so, whether it depends on the patient's current level of motor impairment. In this pilot study, we investigate differences between EEG-BF and EMG-BF for a virtual-reality-based stroke rehabilitation device to identify which type of BF is more suitable for two individuals with different levels of motor impairment following stroke.

Two chronic stroke survivors with mild and severe motor impairment (Fugl-Meyer – Upper Extremity: 37/66 and 13/66) were recruited for preliminary analysis. Data was acquired over sixteen 1.5-hour sessions, eight with each BF modality, using a HMD-VR training paradigm we developed for stroke rehabilitation (REINVENT, see Vourvopoulos et al. 2019), which can selectively provide BF of ipsilesional sensorimotor brain activity (EEG-BF) or paretic muscular activation (EMG-BF). For each trial, participants attempted to move their affected arm. Successful trials, defined as when their EEG sensorimotor desynchronization (8-24 Hz) or EMG mean activity during movement attempt exceeded their preceding resting-state, drove a virtual arm towards a target. A success rate was calculated as the ratio of successful to total trials for each session.

Training performance with EEG-BF for the severely impaired participant increased 7.3 % (73.3 – 80.6 %) between the first and last sessions, while for the mildly impaired participant decreased 5.4 % (65.4 – 60 %); however, there was no significant difference. In contrast, performance with EMG-BF showed an increase of 20.5 % (23.3 - 43.8 %) for the severely impaired participant and no change for the mildly impaired participant (95 %). Further analysis of the EEG signals showed no significant changes in the sensorimotor bands between the first and last sessions for either participant. However, EMG analysis revealed a significant increase in muscular activity for the mildly impaired participant only.

Our preliminary results suggest that VR-BF may have greater efficacy when considering the level of impairment of the stroke participant. The participant with severe motor impairment showed moderate improvements in performance with both BF modalities. In contrast, the participant with mild motor impairment showed a decrease in performance when using EEG-BF and no change in EMG-BF performance, but had higher muscular activity when using EMG-BF, suggesting some benefits. This suggests that BF therapy might be most efficacious if the modality used is tailored to the level of impairment of the patient. However, a greater sample is required to confirm these findings and further investigate thresholds to define the population that would most benefit from each BF modality.

T24: Corticospinal Tract Lesion Load, but Not Lesion Volume, Improves Hippocampal Volume Prediction Model in Chronic Stroke Patients

Artemis Zavaliangos-Petropulu[1,2], Neda Jahanshad[1], Paul Thompson[1], Sook-Lei Liew[2,1]
*[1]Imaging Genetics Center, Mark and Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine, University of Southern California, Marina Del Rey, USA. [2]Neural Plasticity and Neurorehabilitation Laboratory, University of Southern California, Los Angeles, USA*

Hippocampal volumes decrease with age and are associated with cognitive impairment. In the context of stroke motor rehabilitation research, however, the hippocampus has not been widely studied. In particular, the relationship of hippocampal volumes to stroke-related brain injury is unclear. Here we set out to assess how post-stroke brain injury measures, such as lesion volume and lesion load on the corticospinal tract (CST-LL), relate to hippocampal volume. We hypothesized that hippocampal volume is negatively associated with both CST-LL and lesion volume in chronic stroke patients.

T1-weighted volumetric brain MRI scans from the ATLAS data set (N=169 chronic stroke patients across 5 research sites) were processed with FreeSurfer 6.0 to segment hippocampal volume. The Pipelines for Analyzing Lesions after Stroke (PALS) toolbox was used to calculate lesion volume and CST-LL. Outputs were manually inspected and quality controlled. We used mixed effects linear models to test ipsilesional (N=86; age=57.6±12.5 ; M/F=62/24; average motor performance= 0.75±0.28) and contralesional (N=97; age=57.2±12.9; M/F=68/29; average motor performance=0.72±0.28) associations with hippocampal volume. Hippocampal volumes were normalized for intracranial volume using residual correction. Research site was included as a random effect, along with fixed effects of age, sex and lesioned hemisphere. Three separate models evaluated the addition of lesion volume and CST-LL individually (due to collinearity) as fixed effects.

As shown previously, age was negatively associated with both ipsilesional (p=1.1x10^-6; t=-5.3) and contralesional (p=6.5x10^-6; t=-5.9) hippocampal volumes. Although neither of the post-stroke brain injury measures were statistically significantly associated with hippocampal volume, CST-LL substantially contributed to the model fit. CST-LL significantly improved the model predicting both the ipsilesional (ΔAIC=-19.4) and contralesional (ΔAIC=-21.0) hippocampal volume. However, lesion volume significantly worsened both ipsilesional (ΔAIC=12.3) and contralesional (ΔAIC=13.7) hippocampus models.

These findings show that lesion volume alone likely does not contribute to post-stroke hippocampal volumes. However, a more specific measure of the direct impact of the lesion on the corticospinal tract as measured by CST-LL may contribute to post-stroke hippocampal volumes. As CST-LL is a biomarker of post-stroke motor performance and motor recovery, this may provide an initial relationship between post-stroke hippocampal volume with post-stroke motor neurorehabilitation research. Future studies are necessary to evaluate the specific relationships between the hippocampus and CST-LL along with motor performance.

## T25: A Knowledge Base for Human Motor Circuitry

Souvik Roy[1], Kara Bocan[2], Natasa Miskov- Zivanov[2], Wittenberg George[3,4,5]
*[1]University of Pittsburgh School of Medicine, Pittsburgh, USA. [2]University of Pittsburgh Department of Electrical Engineering, Pittsburgh, USA. [3]University of Pittsburgh Department of Neurology, Pittsburgh, USA. [4]Center for Neural Basis of Cognition, Pittsburgh, USA. [5]Rehab Neural Engineering Labs, Pittsburgh, USA*

An improved understanding of the circuits within the human motor system would allow for more specific targeting of interventions to restore motor function impaired by neurological conditions. Information about those circuits is available from the many studies that examine connections between brain regions implicated in human motor function. As of yet, there is no established method to systematically combine these studies to build knowledge of motor networks. We propose a systematic data aggregation approach to mine connectivity data present in the literature regarding connections between motor regions. Our current method focuses on a sample of studies using transcranial magnetic stimulation (TMS) but we will discuss how these methods could be applied to broader knowledge bases. Ultimately the goal of this project is to create an open source, semi-automated database that can drive the construction of graphical models, propose new directions in lesion-symptom mapping, and aid in the generation of hypotheses.

## T26: Gait Abnormality Detection in Patients with Parkinson's Disease

Nader Naghavi, Eric Wade
*University of Tennessee, Knoxville, USA*

### Introduction:

Freezing of gate (FoG), an incapacitating motor dysfunction associated with Parkinson's disease (PD), is a sudden and transient reduction in forward progression. FoG, the main risk factor for falling in patients with PD, negatively affects mobility and independence, causes emotional stress, and reduces quality of life. External cues, as discrete targets for the execution of a movement, can help people to overcome FoG events. The current study compares classifier models designed to detect FoG using wearable sensor data; successful detection can be used to automatically trigger cues to prevent FoG occurrence.

### Materials and Methods:

Eighteen participants with PD (12M/6F, years, Hoehn and Yahr scores from 2-4) walked in at self-selected speeds through a narrow (38ft. × 5ft.) hallway for minutes. They were required to negotiate environmental stimuli such as turns, varied path widths, and unexpected stops. Two accelerometers (APDM Inc., www.apdm.com) were placed on the left and right ankles superior to the tibia/talus joint to collect horizontal (perpendicular to the frontal plane) and vertical (perpendicular to the transverse plane) motion data. Sensor data associated with stops or no activity were excluded to create a dataset of normal gait and FoG. FoG data also included data from 1s pre-FoG periods to enable the system to predict FoG before its occurrence. Using sliding windows of 2s and a step of 0.5s, we extracted four features (freeze index, sample entropy, standard deviation and signal power) from acceleration data (sampled at 128Hz). We compared classification results using two datasets: 1) Each sample included features only from the current window of both sensors and both directions creating an array of 16 elements (D1); 2) Each sample included features of six successive windows ending with the current window creating an array of 96 elements (D6). Finally, we trained and tested three different models to detect FoG: Support Vector Machine (SVM), k-Nearest Neighbors (kNN) and Multilayer Perceptron (MLP). All classifiers were trained and tested by the same set of data including 60% and 40% of the entire dataset, respectively.

### Results and Discussion:

According to the F1 statistic, using features from successive windows (D6) improves FoG detection (91.0%, 89.2% and 87.6% using D6, and 86.1%, 83.5% and 84.5% using D1 for SVM, kNN and MLP, respectively). Also, SVM outperforms the other classifiers (sensitivity = 91.8% and specificity = 98.5% using D6, and, sensitivity =84.8% and specificity = 98.2% using D1).

### Conclusions:

Because FoG develops dynamically, using successive windows of data improves performance of FoG detectors. This model may be useful in the development of a closed-loop system for automatic FoG mitigation. We also suggest using data synthesis methods (e.g. SMOTE) to create a balanced dataset to improve FoG detection.

## T27: Measuring Transcallosal Inhibition for the Lower Extremity: Methodology and reliability in stroke

Anjali Sivaramakrishnan, Sangeetha Madhavan
*University of Illinois at Chicago, Chicago, USA*

### Background:

Transcallosal inhibition (TCI) is a measure of between-hemisphere inhibitory control that is mediated by the corpus callosum. TCI is evaluated either with a paired pulse or single pulse transcranial magnetic stimulation (TMS) paradigm. The ipsilateral silent period (iSP) is an index of TCI where a suprathreshold stimulus is applied to the ipsilateral motor cortex, while the target ipsilateral muscle maintains a tonic contraction. TCI outcome measures quantify the degree of interhemispheric inhibition of voluntary movement, and greater iSP duration typically indicates greater inhibition. Change in TCI can provide insights into pathophysiological mechanisms underlying the asymmetry in corticomotor excitability in stroke. The study of iSP for the lower extremity has been limited, possibly due to the close orientation of the lower extremity motor representations. Here, we describe a method for iSP quantification and measurement for the tibialis anterior muscle in stroke. We also report the reliability of iSP onset latency, duration, and area in stroke survivors.

### Methods:

19 individuals with stroke (mean age 58.8 years, range: 44 - 67) attended three sessions where TCI from the lesioned to non-lesioned hemisphere was measured from the non-paretic tibialis anterior muscle. Single pulse TMS was used with a double cone coil for delivering 8 stimuli to the ipsilateral motor cortex (i.e. affected hemisphere) at 130% active motor threshold, while the participant maintained an isometric contraction at 50% maximum voluntary effort. For analyses, each trial was rectified and iSP onset and offset were determined with 25% mean of pre-stimulus electromyogram (EMG) activity set as limits. We measured iSP onset latency, iSP duration, iSP area, and area relative to background EMG activity (normalized iSP area). Intra-class correlation coefficients (ICC) and coefficients of variation were computed to examine test-retest reliability and variability.

### Results:

The reliability coefficients ranged from moderate to good for all parameters: iSP onset latency (ICC =0.6), normalized iSP area (ICC = 0.6), iSP duration (ICC = 0.77) and iSP area (ICC = 0.81). iSP onset latency showed the least variability (CV ranging from 0.12 – 0.14) and iSP duration showed maximum variability (CV ranging from 0.56 – 1.01).

### Conclusion:

Our results suggest that iSP parameters, particularly iSP duration and area for the tibialis anterior are reliable in stroke. Our findings are important as we provide a guideline for future studies evaluating TCI for lower extremity muscles in stroke and other clinical populations.

## T28: Atypical Motor Evoked Potentials from Single-Pulse Transcranial Magnetic Stimulation in Children with Hemiparetic Cerebral Palsy

Samuel Nemanich[1], Ephrem Zewdie[2], HsingChing Kuo[2], Sunday Francis[1], Colum MacKinnon[1], Gregg Meekins[3], Adam Kirton[2], Bernadette Gillick[1]
*[1]University of Minnesota, Minneapolis, USA. [2]University of Calgary, Calgary, Canada. [3]Tomah VA Medical Center, Tomah, USA*

### Background:

Single-pulse transcranial magnetic stimulation (TMS) of the motor cortex elicits motor evoked potentials (MEP), which can be directly recorded with electromyography. Typical MEP recordings in intrinsic hand muscles are principally thought to reflect fast-conducting corticospinal projections, and thus are typically characterized by short-latency onsets and fast rise times. In children with hemiparetic cerebral palsy (HCP) due to early stroke, maladaptive neuroplastic changes in the brain may result in reorganization of the corticospinal system, and thus alter the morphological and temporal profile of the MEP evoked by stimulation over motor areas. Understanding atypical MEP patterns may help us understand how the brain has reorganized, and inform us of new potential targets for individualized neuromodulation and neurorehabilitation therapies.

### Objective:

Examine MEP characteristics in a sample of children with HCP and typically-developing peers. We hypothesized MEPs from the more-affected hand would have atypical characteristics compared to less-affected hand MEPs.

### Methods:

Thirteen participants with HCP (14.3 ± 3.04 y/o) and five typically-developing participants (14.3 ± 3.3 y/o) were assessed with single-pulse TMS from two different laboratories in the U.S. and Canada. Bilateral surface EMG in either the first dorsal interosseous or abductor pollicis brevis musculature of the hand captured MEPs. Up to 20 trials using a suprathreshold (120% of resting motor threshold) intensity were examined. Variables of interest included initial latency, MEP duration, and number of peaks. Primary comparisons were 1) MEPs recorded in the respective contralateral hand from stimulating the lesioned vs. non-lesioned hemisphere; 2) MEPs recorded in contralateral (less-affected) vs. ipsilateral (more-affected) hand from stimulating the non-lesioned hemisphere, and 3) HCP vs. typically-development.

### Results:

1) Contralateral MEPs from non-lesioned vs. lesioned hemisphere stimulation: Latencies were similar (mean difference = 1.8 ± 2.6 ms), MEP duration was longer (6.1 ± 7.2 ms), and there was on average one additional peak in MEP waveforms obtained from non-lesioned relative to lesioned hemisphere, indicating a multiphasic morphology.

2) Contralateral vs. ipsilateral MEPs from non-lesioned hemisphere stimulation: Latencies were similar (mean difference = -0.51 ± 1.2 ms), MEP duration was longer (7.0 ± 8.5 ms), and there was on average one additional peak in contralateral relative to ipsilateral MEP waveforms.

3) MEP latency was slightly longer for less-affected (22.5 ± 1.6 ms) and more-affected (22.7 ± 2.8 ms) hand MEPs compared to dominant (21.0 ± 0.8 ms) and non-dominant (21.0 ± 1.3 ms) hand MEPs in typically-developing children.

### Conclusions:

Combining data from two different laboratories that employed similar methods to study cortical plasticity in children with HCP, our analysis showed that the MEP characteristics of contralateral projections to the stronger hand were longer in duration and had more complex morphologies. These findings suggest analysis of atypical MEP patterns may be an approach to probe developmental neuroplasticity and reorganization after early brain injury.

T29: Comparison of Corticospinal Tract Fractional Anisotropy Extracted from Native Versus Standard Space in Chronic Stroke

Allison Lewis, Jill Stewart
*University of South Carolina, Columbia, SC, USA*

Fractional anisotropy (FA) of the corticospinal tract (CST) has been suggested as a biomarker of the motor system after stroke. The optimal approach for extraction of FA from the CST is not known with some studies extracting FA from native diffusion space and others from standard space. The purpose of this study was to compare CST FA extracted from native diffusion space to CST FA from standard space after stroke. Twenty-six participants in the chronic phase of stroke (mean age 60.12 ± 9.77, months post-stroke 36.23 ± 36.23, UE FM score 39.54 ± 14.88) underwent diffusion weighted imaging. All data were processed in FSL. CST FA was extracted using two approaches from both native and standard space. For the Cerebral Peduncle approach, FA was extracted from a region of interest (ROI) in the cerebral peduncle. For the Tract Template approach, FA was extracted from a template of the CST. Each approach was repeated in native and standard space. Paired differences between native space FA ($FA_{native}$) and standard space FA ($FA_{std}$) were examined. Relationships between FA (native and standard) and upper extremity motor measures were also examined. As expected, the ipsilesional CST FA was significantly lower than the contralesional CST FA for both approaches, regardless of extraction space (native or standard space) ($p<0.01$). $FA_{native}$ correlated with $FA_{std}$ for the both approaches ($r>0.76$, $p<0.01$). However, CST $FA_{native}$ was significantly different from the CST $FA_{std}$ for the Tract Template approach, but not for the Cerebral Peduncle approach. The directional difference between $FA_{native}$ and $FA_{std}$ was consistent for the Tract Template approach, where $FA_{native}$ was higher than $FA_{std}$ for 25/26 participants. The directional difference between $FA_{native}$ and $FA_{std}$ was not consistent for the Cerebral Peduncle approach, where $FA_{native}$ was higher than $FA_{std}$ for only 12/26 participants. However, the magnitude of the absolute difference between $FA_{native}$ and $FA_{std}$ was similar between the two approaches (ipsilesional CST $FA_{native}$-$FA_{std}$ = 0.019 ± 0.018 for the Cerebral Peduncle approach and 0.014 ± 0.010 for the Tract Template approach; contralesional CST $FA_{native}$-$FA_{std}$ = 0.018 ± 0.013 for the Cerebral Peduncle approach and 0.012 ± 0.007 for the Tract Template approach). The relationships between $FA_{native}$, upper extremity impairment measured by the Fugl-Meyer (UE FM), and upper extremity function measured by the Action Research Arm Test (ARAT) ($r=0.41$-$0.69$; $p<0.05$) were similar to relationships between $FA_{std}$, UE FM, and ARAT ($r=0.44$-$0.60$; $p<0.05$). In conclusion, our results suggest that FA values extracted from native space versus diffusion space may differ, although the magnitude of the difference was small, however, the relationship between FA and motor function was comparable. The results of this study may have implications for how FA can be interpreted across studies that extract data from different spaces.

## T30: Brain Derived Neurotrophic Factor Gene (BDNF) Polymorphism Predicts Response to Continuous Theta Burst Stimulation (cTBS) in Chronic Stroke Patients

***Presidential Award Finalist**

Shreya Parchure[1], Denise Harvey[1], Priyanka Shah-Basak[1], Laura DeLoretta[1], Rachel Wurzman[1], Daniela Sacchetti[1], Olufunsho Faseyitan[1], Falk Lohoff[2], Roy Hamilton[1]

[1]*Laboratory for Cognition and Neural Stimulation, Department of Neurology, University of Pennsylvania, Philadelphia, USA.*

[2]*National Institute for Alcohol Abuse and Alcoholism, National Institutes of Health (NIH), Bethesda, USA*

### Background:

The usefulness of repetitive transcranial magnetic stimulation (rTMS) protocols as a means of modulating clinically relevant neuroplasticity depends largely on the degree to which these approaches induce robust and reliable effects. The high degree of inter- and intra-individual variability observed in response to rTMS protocols such as continuous theta burst stimulation (cTBS) therefore represents an obstacle to its utilization as a treatment for neurological disorders. It has been suggested that polymorphism in the gene coding for brain-derived neurotropic factor (BDNF)—a factor involved in human synaptic and neural plasticity—may influence the capacity for neuroplastic changes that underlie the effects of cTBS and other rTMS protocols. Healthy Val66Val carriers have been shown to respond to rTMS in the expected fashion, while healthy Val66Met carriers showed little or paradoxical effects of the stimulation. This study examines the effects of BDNF polymorphism on the response to cTBS in patients with chronic stroke.

### Methodology:

18 individuals with chronic stroke (10 BDNF Val66Met allele carriers) participated in this study. Participants received cTBS (50 Hz triplets of TMS delivered at 5 Hz) over the hand representation of the primary motor cortex. 30 motor-evoke potentials (MEP) were obtained before cTBS, and post-stimulation at 0, 10, 20 and 30 minutes. The DNA samples were genotyped for BDNF (the single nucleotide polymorphism rs6265) using standard methods. 95% confidence intervals were derived to compare mean log MEP at each time point by genotype, and two-tailed t-tests were used to compare Val66Val and Val66Met carriers.

### Results:

There are significant differences ($p<0.05$) in mean log MEP at 0 and 10 minutes post-cTBS between Val66Val and Val66Met carriers. In addition, Val66Val carriers undergo a significant ($p<0.05$) *decrease* in log MEP at all time points after cTBS compared to baseline. Val66Met carriers show a significant ($p<0.05$) *increase* in log MEP at 10 minutes after cTBS compared to baseline.

### Conclusion:

BDNF genotype status predicted the expected cTBS-induced inhibition of MEPs in stroke patients with the Val66Val allele, whereas patients with Val66Met allele exhibited a paradoxical increase in excitability, with larger MEP elicited after cTBS. Thus, BDNF genotype is a factor that differentially affects neuroplastic responses in individuals with chronic stroke. This provides novel insight into the potential sources of variability in cTBS response in patients, which has important implications for optimizing the utility of this neuromodulation approach. Incorporating BDNF polymorphism genetic screening to stratify patients prior to use of cTBS as a neuromodulatory technique in therapy or research may optimize response rates.

## T31: The Effects of Interval Training with Blood Flow Restriction and Body Cooling on the Cognitive Function of Individuals with Post-Concussive Symptoms for More than One Year

Andrew Stanwicks[1], Caroline Stark[1], Terrie Enis[2], Robert Cantu[2], Jess Gravel[2], Matthew White[2], Yi-Ning Wu[1]
*[1]UMass Lowell, Lowell, USA. [2]Emerson Hospital, The Robert Cantu Concussion Center, Concord, USA*

### Introduction:

Post-Concussion Syndrome (PCS) is a complex disorder in which concussion symptoms last for weeks, months, and even years. Recent research has shown that exercise can improve post-concussion symptoms. Our previous study applying blood flow restriction (BFR) and body cooling (BC) during exercise demonstrated the positive effects such as stable cognitive function recovery on people with PCS less than one year. Persistence of symptoms is a considerable problem even one year after the injury, with cognitive symptoms dominating. This current study aims to examine the effects of 12-session exercise under BFR and BC on people with PCS more than one year.

### Methods:

This ongoing study has recruited eight individuals who have persistent PCS symptoms lasting more than one year with a modified Somatic Perception Questionnaire scored <10. Five participants were assigned to the experimental group and rode a recumbent elliptical machine under BFR and BC (Vasper system, Vasper, Mountain View, CA). Three participants in the control group rode a recumbent elliptical machine (NuStep) without any secondary technologies. All participants followed an interval training program where resistance was varied throughout the session. Evaluations consisting of the Immediate Post-Concussion Assessment and Cognitive Test (ImPACT), Post Concussion Symptom Scale (PCSS), King-Devick test, Balance Error Scoring System (BESS), the Standardized Assessment of Concussion (SAC), and QOLIBRI (quality of life after brain injury) were conducted before and after the 12-session exercise program. PCSS were also acquired daily to assess the trend of PCS symptoms changes. To examine the changes of cognitive function due to the intervention, this abstract focuses on the results of cognitive efficiency index (CEI) of the ImPACT, SAC, and the cognitive symptoms domain of PCSS. Mixed ANOVA was used to test the group differences of CEI, SAC, and symptoms changes.

### Results:

The current results showed that CEI of participants in the experimental group increased significantly higher compared to CEI of those in the control group ($p=0.02$). There was a trend that participants in the experimental group reduced the number of PCS symptoms ($p=0.05$). Additionally, there's a trend that the SAC score increased more compared to SAC scores of the control ($p=0.06$).

### Discussion:

The preliminary results demonstrated that exercise under BFR and BC enhanced the recovery of PCS. CEI and SAC scores showed that symptoms in the cognitive domain improved significantly with the experimental conditions. Recovery in other symptom domains was comparable to conventional exercise.

### Conclusion:

It is feasible to implement interval training as an exercise regimen for people with more than one year persistent PCS symptoms. Interval-training exercise alleviated the post-concussion symptoms of people with PCS. Symptoms in the cognitive domain improved more in the same time period when using BFR and BC.

## T32: Neuroplasticity Following Interlimb Training Differs Between Transradial Versus Partial-Hand Prosthesis Use

Bennett Alterman, William Hendrix, Jade Lee, Katrina Binkley, Emily Keeton, Saif Ali, Lewis Wheaton
*Georgia Institute of Technology, Atlanta, USA*

After upper-extremity amputation, during prosthesis use, it has been shown that there is a maladaptive shift from premotor areas towards increased activity of temporo-parieto-occipital areas of the brain for motor control. This has been attributed to increased visual reliance amid sensory loss from the limb, and may be related to reduced functional outcomes in patients. Leveraging interlimb transfer (ILT)—training with a prosthesis simulator on the sound limb before being fit for the device on the affected limb—it may be possible to diminish this shift in persons with amputation. Through training the intact arm using a prosthesis simulator, there may be opportunity to reinforce the intact networks of motor control. This study seeks to evaluate the utility of ILT in improving neuromotor control of prostheses, and whether there are differences in the effects of ILT between distal (partial-hand) and proximal (transradial) upper-limb prosthesis use. Here, non-amputee participants (n=14) underwent three days of prosthesis training on their non-dominant side between pre-test (day 1) and post-test (day 5) sessions on their dominant side. A control group (n=6) performed only a pre-test (day 1) and follow-up (day 5) test with the prosthesis using their dominant side. Neural data was collected using EEG during the pre- and post-test sessions, and analyzed during movement execution using event-related spectral perturbation (ERSP) analysis. We hypothesized that participants partaking in ILT will show greater changes in ERSP in the mu and beta frequency bands in bilateral sensorimotor regions compared to controls, and that the neurobehavioral effects of ILT will be greater in partial-hand users compared to transradial device users. Results show that before training, there was greater bilateral activation in the beta band (13-30 Hz) in the primary motor cortices in the partial-hand users compared to the transradial users. After interlimb training, activation in the beta band was more strongly lateralized in the partial-hand users to the motor cortex contralateral to prosthesis use. Transradial users showed increased bilateral motor cortex activation from pre-test to post-test. As beta frequency oscillations have been shown to be sensitive to movement and motor skill acquisition, these results suggest differential sensorimotor plasticity after interlimb training mediated by level of limb loss. This work forms the foundation for further examination of neuroplastic changes induced by ILT for potentially enhancing prosthesis adaptation.

## T34: Patient-reported- and Performance-based-measures of Physical Function After Stroke Measure Different Components of Recovery

Margaret French[1], Darcy Reisman[1], Allen Heinemann[2], David Tulsky[1], Daniel White[1]
*[1]University of Delaware, Newark, USA. [2]Shirley Ryan AbilityLab, Chicago, USA*

### Introduction:

Patient-reported outcome measures (PROMs) and performance-based measures (PBMs) of physical function measure different aspects of function in older adults and individuals with orthopedic conditions. Geriatrics and orthopedics now use PROMs and PBMs to track recovery. Post-stroke rehabilitation, however, primarily monitors recovery by PBMs alone. This is evident in the Academy of Neurologic Physical Therapy's Core Set Outcome Measures Clinical Practice Guideline, which recommends six core outcome measures, five of which are PBMs. By overlooking PROMs, neurorehabilitation professionals may miss important aspects of post-stroke recovery. However, the extent to which PROMs and PBMs measuring functional mobility in stroke survivors complement each other has not been examined. Thus, this study aimed to determine the agreement between PROMs and PBMs of functional mobility after stroke.

### Methods:

Individuals with chronic (>6 months) stroke who were able to walk without physical assistance completed the 4-meter-walk-test (i.e., self-selected walking speed; SSWS) from the NIH Toolbox Motor Battery and the Quality of Life in Neurologic Disorders: Lower Extremity scale (Neuro-QOL: LE). We completed a linear regression with the SSWS (i.e., a PBM) as the dependent variable and the Neuro-QOL: LE (i.e., a PROM) as the independent variable. Then, we further assessed agreement between PROMs and PBMs by classifying participants as community ambulators (≥0.8 m/s) or limited ambulators (<0.8 m/s) based on gait speed and as able or unable to walk 15 minutes based on the NeuroQOL: LE item "are you able to go for a walk of at least 15 minutes." We calculated Kappa and 95% Confidence Intervals (95% CI).

### Results:

One-hundred and eighty-one stroke survivors (55.83 ±13.05 yrs, 91 F) were included in the analysis. There was a moderate association between SSWS and Neuro-QOL: LE ($p<0.001$; $R^2=0.37$). Agreement between community ambulation and patient-reported ability to walk for 15 minutes was fair ($\kappa=0.226$; 95% CI 0.12-0.33). Of the 98 participants classified as a community ambulator, 96% (94/98) reported being able to walk for 15 minutes, while only 75% of the 83 participants classified as a non-community ambulator (62) reported being able to walk for 15 minutes.

### Discussion:

A PROM, Neuro-QOL: LE, explained a moderate portion of variability in SSWS (a PBM), suggesting that PROMs and PBMs assess distinct but complementary aspects of community ambulation. The unexplained variance suggests that the experience of people after stroke as measured by PROMs complements performance-based tests. Both PROMs and PBMs contribute to our understanding of post-stroke recovery.

## T35: Implementation and Evaluation of the Graded Repetitive Arm Supplementary Program (GRASP) in the Community

Chieh-ling Yang[1,2], Marie-Louise Bird[3], Janice Eng[1,2]
*[1]University of British Columbia, Vancouver, Canada. [2]GF Strong Rehab Centre, Vancouver, Canada. [3]University of Tasmania, Launceston, Australia*

### Background:

The Graded Repetitive Arm Supplementary Program (GRASP) is a stroke neurorehabilitation intervention shown to improve upper extremity (UE) function under randomized controlled trial settings. However, little is known about how to successfully translate effective evidence-based interventions to "real-world" community settings.

### Aims:

To evaluate the implementation of the GRASP in a community setting using the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework, we 1) identified barriers and facilitators to program implementation and 2) assessed the effects of the GRASP on UE function and quality of life in individuals with stroke.

### Methods:

We established a partnership with the Stroke Recovery Association of British Columbia (SRABC) and a local community centre to deliver the program. University researchers trained staff from SRABC to run the GRASP community program and the community centre provided space and collected fees. The program consisted of 10 weeks of one-hour group class and individualized homework. Stroke participants were approached and consented after they had registered for the program.

### Results:

*REACH*: Twelve people were screened. Eight people were eligible (1 month to 12 years poststroke), and 7 consented to participate in the study. Four people having insufficient voluntary movement in the affected arm/hand were not eligible. *EFFECTIVENESS*: Participants demonstrated significant improvement in the Fugl-Meyer Assessment ($p = 0.036$), grip strength ($p = 0.047$), and the Stroke Impact Scale-Hand Function Domain ($p = 0.022$). Four out of 7 participants showed meaningful changes in affected UE use as measured by the Rating of Everyday Arm-Use in the Community and Home scale. *ADOPTION*: All people who met the eligibility criteria participated in the program. Common facilitators to program uptake were that the program was just for stroke patients, the intention to improve their arm/hand function, and affordable cost ($5/session). Common barriers to doing GRASP were that exercises could be boring, difficult, and fatiguing. *IMPLEMENTATION*: The program was implemented as intended as verified by the fidelity checklist during in-class observations. Main challenges to delivering the program were to accommodate participants with different levels of arm/hand function and to utilize effective approaches to facilitate the group. The average attendance was 6.3 classes (SD=1.16), with 75% of participants attending ≥80% of classes and the average GRASP practice time was 59 mins/day (SD=15.49). *MAINTENANCE*: Both the partner organization and community centre continued offering the program in the next term.

### Conclusions:

The GRASP community program was successfully implemented in a community setting, delivered by staff from the SRABC trained by University researchers. The program was effective in improving several measures of UE function and quality of life. This model of partnership development may be useful for other rehabilitation interventions and serve as the first step for future larger-scale implementation of the GRASP.

## T36: Motor Recovery and Sleep after Brain Injury

Melanie K. Fleming[1,2,3], Tom Smejka[1,2], David Henderson Slater[2,1], Veerle van Gils[1,4], Emma Garratt[3], Ece Yilmaz-Kara[2,1], Heidi Johansen-Berg[1]

*[1]Wellcome Centre for Integrative Neuroimaging, University of Oxford, Oxford, United Kingdom. [2]Oxford Centre for Enablement, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom. [3]Oxfordshire Stroke Rehabilitation Unit, Oxford Health NHS Foundation Trust, United Kingdom. [4]Faculty of Psychology and Neuroscience, Mastricht University, Maastricht, Netherlands*

### Introduction:

Sleep plays an important role in consolidation of motor learning, a key component of motor rehabilitation. Brain injury may affect sleep continuity and patients commonly complain of tiredness, daytime sleepiness and increased need for sleep. If sleep is impaired following brain injury, then consolidation of motor skills gained through physical rehabilitation may be suboptimal. This study therefore aims to assess the relationship between sleep quality and motor recovery in stroke and brain injury patients receiving specialist inpatient rehabilitation.

### Methods:

Patients with stroke or brain injury are recruited from two specialist inpatient rehabilitation units as soon as possible after admission. Inclusion criteria: acquired brain injury (stroke, traumatic or hypoxic brain injury, subarachnoid haemorrhage) receiving motor rehabilitation (upper and/or lower limb). Exclusion criteria: inability to provide informed consent; other neurological or psychiatric conditions. Sleep quality and motor function is assessed up to three times throughout the inpatient stay, depending on the length of stay, and functional independence is assessed at admission and discharge. Healthy, age-matched controls are recruited from the community, and their sleep quality is assessed once only. Sleep quality is assessed objectively using actigraphy (7 nights) and subjectively using the Sleep Condition Indicator. Motor outcome assessments include: Action Research Arm test (upper limb function), Fugl Meyer assessment (motor impairment), Rivermead mobility index (RMI) and the Functional independence measure (FIM).

### Results:

Preliminary analysis (37 patients, 49 controls) indicates a lower subjective sleep quality ($p<0.001$), more time spent trying to sleep ($p<0.001$) and higher time awake during the night ($p<0.001$) for inpatients compared with controls. For inpatients there is a negative correlation between average sleep fragmentation and Fugl Meyer and RMI score at discharge ($r=-0.58$, $p=0.02$ & $r=-0.73$, $p=0.005$), rate of recovery of mobility ($r=-0.75$, $p=0.003$) and rate of change in FIM ($r=-0.5$, $p=0.004$).

### Discussion:

Current indications suggest impaired sleep continuity in stroke and brain injury patients receiving inpatient rehabilitation. Sleep quality may correlate with motor outcome and recovery of functional independence. Further data collection is warranted to enable regression analysis.

## T37: Altered Upper Limb Motor Modules and Their Contribution to Post-Stroke Limitations in the Feasible Force Space

Jinsook Roh[1], Gang Seo[1], Sang Wook Lee[2], Amani Alamri[3], Randall Beer[4], Preeti Raghavan[5], Yi-Ning Wu[6], William Rymer[4]
*[1]University of Houston, Houston, USA. [2]Catholic University of America, Washington, USA. [3]WuXi Advanced Therapies, Philadelphia, USA. [4]Northwestern University, Chicago, USA. [5]Johns Hopkins University, Baltimore, USA. [6]University of Massachusetts Lowell, Lowell, USA*

Previous studies suggest that activation of a few motor modules (patterns of muscle activity that flexibly combine to produce motor behaviors) underlies voluntary isometric force generation in stroke survivors, and in neurologically intact individuals. Our prior study demonstrated that stroke altered the composition of these motor modules so that activation of shoulder muscles is abnormally coupled. As we limited our earlier analysis to muscle activation underlying stable target matching phase of 3-D force production, it remains unclear how force is generated during the 'dynamic' or time-varying phase of force generation, as the subject converges to a solution. Thus, we tested the following hypotheses: (1) stroke-specific motor modules are activated from the onset of force generation, instead of emerging in the course of force development; (2) stroke-specific motor modules would relate to altered force representation; and, (3) the altered force representation would limit the feasible force space. EMGs were recorded from eight major muscles of the affected arm of eight chronic hemispheric stroke survivors (Fugl-Meyer UE scores < 25) and from both arms of six age-matched control subjects, during a 3-D isometric force-matching task. A non-negative matrix factorization algorithm identified motor modules in four time-windows: three 'exploratory' force ramping phases (0-33%, 33-67%, and 67-100% of target force magnitude; Ramps 1-3, respectively), and stable force match. The similarity of motor modules was calculated between different epochs of force development and between the two groups. Force components were regressed by the activation coefficients of motor modules and the feasible force space was simulated based on the relationship between the module activation and the end-point force. In each group, the same set of motor modules was present during the four phases of force generation, meaning that stroke-specific modules were activated from the onset of force development. In stroke, the end-point force representation of the abnormal co-activation of the three heads of the deltoid was altered to represent lateral but not downward force. In addition, the set of four post-stroke modules could generate a smaller feasible force space as compared to that of the control group. More specifically, the motor modules of the stroke group did not represent the sub-force space, a combination of lateral, forward, and upward directions. This was identified in our prior study to show that more than 40% of recruited stroke participants could not match these targets without compensatory lateral arm rotation. Overall, the findings suggest that the abnormality in the composition of motor modules and their activation appears to have contributed to the performance degradation post-stroke throughout the voluntary task.

## T38: Development of a Quantitative Tool to Measure Ankle Proprioception in Stroke Survivors

Ahlam Salameh[1,2], Margaret Skelly[1], Jessica Mccabe[1], Svetlana Pundik[1,2]
*[1]Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, USA. [2]Case Western Reserve University, Cleveland, USA*

Purpose:
Ankle proprioception plays an essential role in balance control and gait performance, and is often a significant contributor to disability in stroke. However, current proprioception assessment techniques lack sensitivity to detect deficits and capability to reliably quantify these deficits. Therefore, we developed a quantitative method to assess proprioception of the ankle joint. The purpose of this project is to describe implementation of the Ankle Proprioception Measurement Tool (APMT) with healthy individuals and patients with stroke.

Methods:
Sixteen healthy subjects and seven stroke survivors with chronic motor deficits were evaluated with APMT. While seated, the participants' foot was placed in the apparatus with the axis of rotation of the ankle joint aligned with that of the apparatus. The joint was passively moved up or down by 5°, 10°, or 20° using a pseudo-random list of values. The speed of the ankle movement was ~ 20°/sec. The test was repeated for 20 trials and between each trial, the ankle joint angle was reset back to the center point. During testing, participants view of their foot was obstructed. Participants reported the perceived direction and magnitude of the movement of their ankle joint while referencing a mock scale of displacements. We calculated the average error in degrees and percent of trials with error in direction. For healthy individuals, the protocol was tested on their dominant foot and repeated by two testers. For stroke survivors, we tested both stroke-affected and unaffected sides. We used paired non-parametric statistics for data analysis.

Results:
Controls were 40.4±15.7 years old, and 56% were female. Stroke patients were 65.3±7.5 years old, 57% female, and were 81.9±67.2 months post stroke. The average error in degrees was 0.84±0.79° for controls, 2.82±1.77° for stroke participants' un-affected foot and 3.07±2.40° for the stroke-affected foot. Percent of trials with error in direction was 0% for controls, 0.7±1.9% for the unaffected side and 5.7±8.4% for the stroke-affected side. . There was no difference in results obtained by the two testers (p=0.3936).

Conclusion:
APMT is a potentially useful tool to quantify ankle proprioception. Our results suggest that the APMT discriminates proprioception deficits between healthy controls and stroke survivors but additional research needed to confirm these findings.

T39: The EEG Power Spectrum as a Possible Biomarker for Age-Related Cognitive Decline: A pilot study

Anupriya Pathania, Mindie Clark, Rhiannon Cowen, Matt Euler, Kevin Duff, Keith Lohse
*University of Utah, Salt Lake City, USA*

As we age, numerous neurophysiological changes result in a decline in cognitive and motor abilities. Despite this general declining trend, there is much variability in individual trajectories. Neurotypical aging encompasses a wide range of cognitive abilities, and pathological aging can range from mild cognitive impairment (MCI) to dementia. Given this variability amongst individuals, it is important that we find suitable measures to predict age-related cognitive declines. Some evidence suggests that the slope of the power spectrum in electroencephalography (EEG) may be sensitive to "neural noise" that increases with age. Lower frequencies are dominant in the healthy human EEG spectrum. Under the neural noise hypothesis of aging, if anatomical circuits deteriorate, then the integrity of neuro-oscillations will decay as well, leading to a flatter power spectrum at the physiological level. To investigate the EEG spectral slope with respect to age, we collected EEG before and during the administration of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) in healthy younger and older adults.

Twenty-five participants were recruited from the university community for this pilot study: healthy young adults (YA; <35 y; n = 21) and cognitively healthy older adults (OA; >65 y; n = 4). None of the participants had diagnosed cognitive impairments or psychiatric conditions. Participants were also free of perceptual or motor deficits that would interfere with their ability to complete the RBANS. The RBANS was administered by a trained research assistant, and all subtests (immediate memory; visuospatial and constructional abilities; attention; language; and delayed memory) were assessed in the lab. Resting and on-task EEG data were collected with a 32-channel BrainVision ActiCAP system.

Linear mixed-effects regression analysis revealed that flatter spectral slopes were associated with older age ($p = 0.002$), consistent with the neural noise hypothesis of aging.  Age was not a statistically significant predictor for any of the subtests of the RBANS, although coefficients were generally negative. However, there was an Age x Spectral Slope interaction ($p = 0.028$) for the digit span test, such that digit span performance generally declined with age, but this decline was greater for participants with a flatter spectral slope. No other effects for the different subscales were statistically significant.

These data showed that the spectral slope became more positive (i.e., flatter) with an increase in chronological age. Additionally, the significant interaction for the digit-span task suggests that flatter spectral slopes are associated with worse cognitive performance controlling for age. This pilot study is limited by its small sample size and several exploratory statistical tests for the different subscales of the RBANS. The initial data are compelling, however, and future research should replicate these effects in a larger sample of healthy older adults before clinical research is undertaken.

## T40: Enhancing Motor Recovery with Two Types of Intense and High-Dose Training in the Sub-Acute Period After Stroke: The SMARTS2 study

John Krakauer[1], Tomoko Kitago[2,3,4], Jeff Goldsmith[3], Omar Ahmad[1], Promit Roy[1], Joel Stein[3], Lauri Bishop[5,3], Kelly Casey[1], Belen Valladares[6], Michelle Harran[1,3], Juan Camilo Cortes[1,3], Forrence Alexander[1], Jing Xu[1], Sandra DeLuzio[1], Benjamin Hertler[6], Jeremia Held[6], Bert Eenhoorn[6], Levke Steiner[6], Kelly Jordan[7], Daniel Ludwig[1], Megan Moore[7], Marlena Casey[1], Isha Vora[1], Steven Zeiler[1], Meret Branscheidt[8], Gert Kwakkel[10], Andreas Luft[6,11]

*[1]Johns Hopkins University, Baltimore, USA. [2]Burke Neurological Institute, White Plains, USA. [3]Columbia University, New York, USA. [4]Weill Cornell Medicine, New York, USA. [5]University of Southern California, Los Angeles, USA. [6]University Hospital Zurich, Zurich, Switzerland. [7]Johns Hopkins University, White Plains, USA. [8]University Hospital Zurich, Zurich, USA. [10]Amsterdam University Medical Center, Amsterdam, Netherlands. [11]Cereneo Center for Neurology and Rehabilitation, Vitznau, Switzerland*

Current neurorehabilitation approaches have been ineffective in enhancing early spontaneous recovery from motor impairment after stroke. Recent work in chronic stroke has shown promising results at both the activity and impairment levels with increased intensities and doses of task-oriented therapy.

SMARTS2 was a multicenter, single-blinded, randomized controlled trial in subacute stroke, comparing the efficacy of intensive conventional task-oriented therapy (COT) with a new non-task-oriented approach emphasizing quality of movement execution in an immersive gaming environment (GT). The hypothesis was that GT would be superior to COT at reducing impairment and at least as good at improving activity. The secondary hypothesis was that both would be better than conventional levels of neurorehabilitation. In the GT group, patients made 3D arm movements while playing a custom videogame using the ArmeoPower device to unweight the arm. Patients with ischemic stroke (n=21, 11F/10M, aged 63.8±12.5 years, enrolled 20.1±13.1 days post-stroke) were randomized 1:1 to GT or COT. The target schedule was two 60-minute sessions daily, 5 days per week for 3 weeks. The primary outcome was the change in Fugl-Meyer Upper Extremity score (FM) from baseline to day 3 post-training. Secondary outcomes included Action Research Arm Test (ARAT), reaching kinematics, and finger individuation.

Age, time post-stroke, and baseline FM and ARAT scores were not significantly different between groups. Patients in both groups demonstrated increases in FM scores from baseline to day 3 post-training (GT 12.5±2.2; COT 13.4±2.28) with no significant difference between groups (p=0.77). There were also no significant differences between groups for the change in ARAT (GT 13.4±3.0; COT 14.7±3.2; p=0.77), reaching kinematics (measured in $AMD^2$; GT -31.0±8.12; COT -19.3±17.6; p = 0.63), or for finger individuation (GT 0.22±0.08; COT 0.19±0.08; p = 0.81).

Secondary analysis compared FM and ARAT changes in our study (combined GT and COT groups) with historical controls from the EXPLICIT trial over a similar time period post-stroke. We found that ARAT changes, but not FM changes, in our intensive therapy trial were significantly larger than in controls matched by time post-stroke and stroke severity.

In conclusion, there was no difference in motor recovery between the two intensive therapy groups in our study. The comparison to historical controls revealed that higher intensities and doses of therapy, whether through our novel gaming paradigm or COT, is able to add to spontaneous recovery and is superior to current standard of care. The fact that a novel gaming therapy did as well as COT is promising, as technology lends itself to further optimization. The dissociation between the effect of intensive therapy on ARAT versus FM may speak to the difference in the responsiveness to therapy of negative and positive features of hemiparesis.

## T41: Comparison of Between Arm Muscle Activation During Unilateral Reaching in Individuals with Pediatric Hemiplegia

Nayo Hill, Julius Dewald
*Northwestern University, Chicago, USA*

### Introduction:

An early, unilateral lesion to the developing brain, resulting in pediatric hemiplegia (PH), can limit an individual's ability to individually control their upper extremities. Previous work provides evidence of bilateral elbow torque production during non-paretic arm elbow flexion/extension tasks in individuals with PH. The goal of this current work is to characterize the presence of between arm muscle activity during a dynamic, multi-joint reaching task to gain insight into descending motor commands in individuals with lesions to the developing brain.

### Methods:

With the arm rigidly coupled to a robotic device, individuals completed ballistic reaches to a virtual target. Reaches were completed with full support of a haptic table and while generating 20 to 80% of maximum voluntary shoulder abduction torque to modulate descending drive required for the task. EMG activity from the lateral head of the triceps and intermediate deltoid was recorded bilaterally during the reach. The magnitude and time point of maximum EMG activity was isolated for each muscle on the reaching arm. Activity of the corresponding muscle on the non-reaching arm was isolated for the same time point to quantify simultaneous bilateral activity. Muscle activity was normalized to maximum voluntary contractions recorded isometrically prior to the reaching trials. The EMG laterality measure was calculated to compare the amount of normalized muscle activity in the test arm to simultaneous activity in the non-test arm. A value of 1 indicates all test arm EMG activity and no non-test arm EMG activity, a value of 0 indicates equal activity between arms, and a value of -1 indicates all non-test arm EMG activity. Reaching tasks were completed by both arms for comparison.

### Results:

Participants included one individual with a periventricular lesion acquired in utero (PRE), one individual who sustained a perinatal middle cerebral artery stroke around full term (PERI), and one typically developing control (TD). The dominant arm corresponds to the non-paretic arm for participants with PH. EMG activity in the lateral head of the triceps and intermediate deltoid increased with shoulder abduction load in both arms for all participants. For the table support condition, EMG laterality for the deltoid (dominant, non-dominant) was TD(0.96, 0.89), PRE(0.66, 0.93), and PERI(0.10, 0.97). For the highest load condition, laterality for the deltoid was TD(0.86, 0.69), PRE(0.26, 0.91), and PERI(0.11, 0.92).

### Conclusions:

When reaching with the non-paretic arm, individuals with PH demonstrate large amounts of bilateral muscle activity that is not present when reaching with the paretic arm. This finding indicates an impairment in individual muscle activation between limbs during a single arm task in these individuals with PH compared to a control. Additional research is necessary to understand the neurological mechanisms contributing to the present findings.

## T42: Further Consensus building at the Second Stroke Recovery and Rehabilitation Roundtable (SRRR II)

Julie Bernhardt[1,2], Kathryn Hayward[1,3,2], Gert Kwakkel[4,5], Jane Burridge[6], Janice Eng[7], Marion Walker[8], Marie-Louise Bird[7,9], Karen Borschmann[1,2], Steven Cramer[10], Michael O'Sullivan[11], Andrew Clarkson[12], Matthew McDonald[13,14], Matthew Jeffers[13,14], Dale Corbett[13,14], On behalf of the SRRR II Collaboration

*[1]Florey Institute of Neuroscience and Mental Health, Melbourne, Australia. [2]NHMRC CRE in Stroke Rehabilitation and Brain Recovery, Melbourne, Australia. [3]University of Melbourne, Melbourne, Australia. [4]Amsterdam UMC Vrije Universiteit, Amsterdam, Netherlands. [5]Amsterdam Rehabilitation Research Centre, Amsterdam, Netherlands. [6]University of Southampton, Southhampton, United Kingdom. [7]The University of British Columbia, Vancouver, Canada. [8]University of Nottingham, Nottingham, United Kingdom. [9]University of Tasmania, Hobart, Australia. [10]University of California Irvine, Irvine, USA. [11]University of Queensland, Brisbane, Australia. [12]University of Otago, Otago, New Zealand. [13]University of Ottawa, Ottawa, Canada. [14]Canadian Partnership for Stroke Recovery, Ottawa, Canada.*

### Background:
The Stroke Recovery and Rehabilitation Roundtables (SRRR) bring together an international group of clinical and pre-clinical researchers, methodologists, funders and consumers. We aim to accelerate development, and facilitate implementation, of effective treatments to enhance recovery after stroke. SRRR I (USA, May 2016) focused on 4 areas: (i) preclinical translation; (ii) recovery biomarkers; (iii) intervention development, monitoring and reporting standards; and (iv) standardised measurement in motor recovery trials. SRRR II (Canada, October 2018) aimed to create pathways to realise key objectives and targets identified in SRRR I. The 2018 working groups focused on developing consensus recommendations in the following areas: (i) cognitive impairment post stroke; (ii) standardising measurement of movement quality; (iii) improving development of recovery trials; and (iv) moving knowledge into practice. The aim of this abstract is to provide an overview of the consensus-based recommendations achieved by each group.

### Methods:
Across the four working groups, we had 38 core and 42 extended advisory group members. Groups were multidisciplinary and international (members from >15 countries). Working groups met via videoconference over the 12 months preceding our face-to-face meeting that occurred over two days in October 2018. Consensus building methods included online surveys and graph theory-based voting systems. Each group produced a list of recommendations for consideration in future stroke recovery and rehabilitation work.

### Results:
Recommendations to advance the science of recovery research were identified by each group: (i) cognitive impairment post stroke n = 10 recommendations; (ii) standardising measurement of movement quality n = 6 recommendations; (iii) improving development of recovery trials n = 8 recommendations; and (iv) moving knowledge into practice, n = 4 recommendations. Additional outputs to support uptake of the recommendations included conceptualisation of neurocognitive domains and neural correlates; protocols for performance assays and a functional task; SRRR Trials Development Framework; and collation of resources supporting protocols for implementation.

### Discussion:
The SRRR has united participants who are committed to progressing stroke recovery and rehabilitation science and practice, and building strong, international partnerships to accelerate change. All recommendations are co-published in the International Journal of Stroke and Neurorehabilitation & Neural Repair. We hope that researchers, clinicians and academics in the field of stroke recovery, together with funding bodies and journal editors, will join us in pursuing and promoting the recommendations defined by the SRRR I and II working groups, which support our vision for change. The next step is formation of an International Stroke Recovery and Rehabilitation Alliance (ISSRA), where new working groups will take recommendations and build partnerships to accelerate action to advance our goals.

T43: Development of a Novel EMG Controlled Force Tracker Task to Study Motor Learning in Chronic Stroke

Emily L. Hinson[1], Melanie K. Fleming[1], Fylis Van Horssen[2], Alek Pogosyan[1], Will Clarke[1], Charlotte J Stagg[1]
*[1]University of Oxford, Oxford, United Kingdom. [2]Radboud University, Nijmegen, Netherlands*

Background:
Motor rehabilitation for stroke survivors is frequently informed by research of motor learning in healthy controls, however it is not fully established if stroke survivors learn motor skills in the same way, therefore potentially questioning the validity of basing rehabilitation techniques on these models. Furthermore, motor learning tasks performed in stroke cohorts are hampered by floor/ceiling effects when compared to healthy controls. This project aims develop and test a novel adaptation of a Force Tracker Task in chronic stroke survivors and age-matched controls.

Methods:
Chronic stroke survivors (minimum 6-months post-stroke), age-matched controls and young healthy controls (aged 18-35) completed an EMG controlled Force Tracker Task (EMG-FTT), controlled using modulated contraction and relaxation of the forearm extensor muscle (affected/non-dominant arm). Structural, functional and spectroscopic MRI scanning will be performed on the same day (prior to motor task performance) in chronic stroke survivors and older adults.

Results:
Behavioural data from young healthy controls show that participants are able to decrease error during training on the EMG-FTT.  Preliminary results in chronic stroke survivors and older adults show that older adults show a similar performance to young adults, with both groups able to perform, and decrease error. Further analysis will explore relationships between individual behavioural performance with measures from the MRI session. We predict that we will be able to replicate previously observed relationships between behavioural performance and neurotransmitter systems in healthy controls and we will look to investigate if these relationships hold for stroke survivors.

Discussion:
Many motor learning tasks performed with stroke and age-matched cohorts are limited by floor/ceiling effects driven by functional ability of the patient cohort. The EMG-FTT is not reliant on a minimum residual functional ability of a stroke survivor and therefore able to assess learning ability in a wider range of stroke survivors. Understanding the learning process post-stroke is crucial to the development of effective rehabilitation strategies.

## T44: Kinematics from Robotic Rehabilitation After Stroke Correlate Motor Recovery Scales

Donghwan Hwang, Suncheol Kwon, Joon-Ho Shin
*National Rehabilitation Center, Seoul, Republic of Korea*

### Purpose:
This study aimed to analyze the correlation the Fugl-Meyer Assessment (FMA) score and a set of clinically useful kinematic features derived from the post-stroke patient's upper limb reaching tasks.

### Methods:
11 patients with cerebral infarction and 9 patients with cerebral hemorrhage participated in upper limb rehabilitation using robotic devices (Armeo®Power and Armeo®Spring, Hocoma, Switzerland) for 4 weeks. The reaching tasks for the assessment of upper limb functions was performed on 0, 14 and 28 day from the starting day of the rehabilitation.

The patients performed the reaching tasks to target points located in lateral, middle, and medial directions for a distance of 75% of the patient's arm length. The three-dimensional trajectory of index fingertip during the tasks was measured using the magnetic tracking system (trakSTAR, Ascension Technology Corp, USA). We calculated 11 kinematic features (Maximum velocity, Hand path ratio, Movement deviation, Target error, Spatial overshoots in horizontal, vertical and sagittal plane, Ratio between mean and maximum velocity, Mean arrest period ratio, Spectral arc length, and Time to velocity peak) from the measured trajectories. Simple linear regression of between FMA score and each feature was performed. Multiple linear regression of between FMA score and the features was then performed.

### Results:
7 kinematic features (Maximum velocity, Mean velocity, Spatial overshoots in horizontal, vertical and sagittal plane, Mean arrest period ratio, and Time to velocity) extracted by linear regression. The results of the analysis showed the correlation between FMA score and the features in the lateral direction ($R^2$=0.632, p<0.01). It showed relatively lower correlation in the middle direction ($R^2$=0.431, p<0.01) and medial direction ($R^2$=0.531, p<0.01).

### Conclusions:
This study analyzed kinematic features of post-stroke patient's upper limb movement. The result indicates that extracted 7 features in the lateral direction relatively high correlate FMA score. We plan to further analysis relationship between reaching direction and motor function of clinical assessments.

## T45: Elucidating the Mechanisms of Cervical Transcutaneous Spinal Stimulation

***Fletcher H. McDowell Award Finalist***

Jaclyn Wehct, Jonah Levine, Hannah Sfreddo, James LiMonta, Yu-Kuang Wu, Noam Harel
*James J. Peters VA Medical Center, Bronx, USA*

### Introduction:

Electromagnetic stimulation facilitates activation of spared neural circuits after spinal cord injury (SCI). With this goal in mind, we apply a novel method of cervical transcutaneous spinal stimulation (cTSS) that activates nerve roots across multiple myotomes in both upper extremities simultaneously. We aim to better understand cTSS mechanisms so that cTSS can eventually be applied in optimal fashion to improve recovery of hand function.

### Methods:

Participants with chronic cervical SCI and able-bodied volunteers underwent transcutaneous stimulation delivered over the ~C4-C5 levels anteriorly and ~T2-T4 levels posteriorly. To understand cTSS circuit interactions, we measured the effects of cTSS paired at varying latencies and stimulus intensities with peripheral nerve stimulation (PNS) or with volitional hand/wrist movement. We also utilized transcranial magnetic stimulation (TMS) paired with volitional movement to further our understanding of the silent period. Outcomes included: effect of subthreshold cTSS on median or ulnar nerve F-wave persistence; effect of suprathreshold cTSS on collisions with median and ulnar nerve F-waves; effect of cTSS on median H-reflex amplitude; effect of cTSS on concurrent volitional muscle contraction; and effect of TMS on concurrent muscle contraction.

### Results:

When subthreshold cTSS was paired with volitional movement we did not see an obvious facilitation of volitional muscle activation. However, when suprathreshold cTSS was paired with volitional movement, a brief relative suppression of activity was often observed, signaling a spinal silent period. The relative spinal silent period was shorter than the silent period observed when TMS is paired with volitional movement. The TMS-induced silent period is composed of both spinal and cortical components. In our experiments, we have found that SCI participants experience a shorter TMS-induced silent period (84.3ms; n=7) relative to their able-bodied counter parts (109.3ms; n=12). Updated results of these and collision experiments between cTSS and F and H waves will be presented.

### Conclusion:

Our novel approach to cervical transcutaneous spinal stimulation provides both mechanistic insight and potential therapeutic application toward upper extremity muscles after SCI. Multiple lines of evidence support the interpretation that this cTSS configuration can activate either spinal sensory afferent or motor efferent pathways. The information gained from the spinal and cortical silent periods provides a pathway to greater understanding of peripheral and central inhibitory mechanisms.

### Support:

New York State DOH C30599; New York State DOH C31291; Craig H. Neilsen Foundation 457648.

## T46: A Comprehensive Assessment of Impairment (Flexion Synergy Pattern) Around the Elbow in Stroke: Preliminary findings from the re-arm study

Levinia van der Velden[1,2], Bram Onneweer[1,2], Joyce Benner[1], Claudia Haarman[3], Marij Roebroeck[1,2], Gerard Ribbers[1,2], Ruud Selles[1,2]
*[1]Erasmus MC University Medical Center, Rotterdam, Netherlands. [2]Rijndam Rehabilitation, Rotterdam, Netherlands. [3]Hankamp Rehab, Enschede, Netherlands*

### Introduction:
To overcome the limitations of clinical assessment tools, such as low inter-rater agreement, poor validity and lack of detailed information, many different robotic devices have been developed to obtain more reliable, valid and operator-independent measurements. However, these devices generally quantify only one or two impairments simultaneously, such as only spasticity and changes of viscoelasticity or only abnormal synergy. We recently developed a Shoulder Elbow Perturbator (SEP), a single robot device that can identify and quantify these different properties. In this study, we provide preliminary results on quantifying abnormal flexion synergy around the elbow in stroke patients and compare them to healthy controls.

### Methods:
The hemi-paretic upper limb of twelve post-stroke patients, three patients with abnormal synergy and ten patients without abnormal synergy as quantified by a low BFM score and the non-dominant upper limb of twelve healthy control subjects were measured in a one degree of freedom haptic manipulator. All subjects performed three active elbow extension movements from maximum flexion to maximum extension under five different vertical arm support-levels. We characterize the synergy pattern by describing the maximum elbow extension level as a function of the arm support level. The hypothesis is that patients with abnormal flexion synergy will show a stronger reduction in maximum extension angle when arm support level decreases.

### Results:
Our preliminary findings show that the three stroke patients with clinical signs of abnormal synergy show a mean decline of 9 degrees and the ten stroke patients without abnormal synergy show a mean decline of 3 degrees when decreasing the arm support level from 100 to 0%. Whereas, the thirteen healthy controls show a mean decline of 1 degree. The between-subject standard deviation in the patient group with abnormal synergy (± 0.050) and without abnormal synergy (± 0.042) was much larger than in the healthy controls (± 0.007).

### Conclusion:
This study presents preliminary findings on a Shoulder Elbow Perturbator to objectively quantify abnormal flexion synergy in stroke. Our findings indicate that indeed the maximum elbow extension level decreases in patients with abnormal flexion synergy when the arm support level decreases. The larger between-subject standard deviation in the patient group may reflect the larger heterogeneity in the stroke patients compared to the controls. In future studies, we will continue to quantify spasticity, viscoelastic properties and muscle weakness with the same experimental setup in larger patient groups to identify the interaction and correlation between impairments.

### Acknowledgements:
The authors would like to thank Hankamp Rehab, Health Holland and Rijndam rehabilitation (hand therapist) for building the SEP and providing financial support to this project.

## T47: Upper Extremity Motor Assessment and Neuroimaging Factors Important for Discharge Destination after Acute Stroke

David Lin[1], Kimberly Erler[2], Kelly Sloane[1], Alison Cloutier[1], Julie DiCarlo[1], Nicole Lam[2], Kristin Parlman[1], Jessica Ranford[1], Seth Finklestein[1], Teresa Kimberley[2], Lee Schwamm[1], Steven Cramer[3], Leigh Hochberg[1]
*[1]Massachusetts General Hospital, Boston, USA. [2]MGH Institute of Health Professions, Boston, USA. [3]University of California Irvine, Irvine, USA*

### Background and Purpose:
Prior studies have shown that sociodemographic factors and functional assessments influence discharge destination after acute stroke. Assessments of upper extremity motor impairment and structural neuroimaging, which are known to be important for motor recovery, have not traditionally been incorporated into discharge decision making. Here we sought to determine whether standardized motor recovery assessments and structural neuroimaging factors including lesion volume, white matter hyperintensity burden, and corticospinal tract injury influence discharge destination for patients with upper extremity weakness after acute stroke.

### Methods:
Upper extremity Fugl-Meyer (UE-FM), Grip Strength (via dynamometer), NIH Stroke Scale (NIHSS) as well as functional assessment (via Barthel index) were collected on patients with upper extremity weakness after ischemic stroke prior to discharge from their acute stroke hospitalization. Lesion volume, white matter burden (Fazekas scale), and corticospinal tract (CST) injury were quantified from images obtained as part of the stroke standard-of-care workup. Kruskal-Wallis tests were run to determine if there were differences between three levels of discharge destination: inpatient rehabilitation facility (IRF), skilled nursing facility (SNF), and home. Binomial logistic regression using behavioral and neuroimaging characteristics was performed to predict discharge to home versus institution (IRF or SNF).

### Results:
In a total sample of N = 86 patients with upper extremity weakness after stroke, 60 were discharged to IRF, 9 to SNF, and 17 home. In addition to Barthel Index ($\chi^2 = 30.3$, $p < 0.001$), there were statistically significant differences between discharge groups on UE-FMA ($\chi^2 = 17.2$, $p<0.001$), grip strength ($\chi^2 = 23.3$, $p<0.001$), NIHSS ($\chi^2 = 19.5$, $p<0.001$), and Fazekas scale ($\chi^2 = 9.3$, $p<0.01$). A logistic regression model including these factors classified 88% of cases and explained 54.3% of the variance in discharge destination. NIHSS, grip strength, and degree of white matter hyperintensity were independently significant. There were no differences between discharge groups on lesion volume and CST injury.

### Conclusions:
Overall stroke severity, white matter hyperintensity burden, and distal hand strength independently predict discharge destination for patients with upper extremity weakness after acute stroke. Notably, measures known to be important for upper extremity recovery in the first three months (UE-FMA and corticospinal tract lesion load) did not predict discharge destination, suggesting that neurologic factors maximally important for recovery are not currently being incorporated into discharge decision making. Future studies that incorporate such measures represent an opportunity for personalizing neurorehabilitation.

## T48: Monoaminergic Drive Upregulates the Expression of the Post-Stroke Flexion Synergy

Jacqueline R. Patterson, C.J. Heckman, Julius P.A. Dewald
*Northwestern University, Chicago, USA*

The role of descending monoaminergic drive in human motor control, particularly following the loss of corticofugal projections, is still largely unknown. Animal work indicates that monoamines modulate the gain of spinal motoneurons. Evidence suggests that following a stroke-induced loss of cortical inputs to the cord and brainstem, a subsequent increase in monoaminergic drive may abnormally increase the gain of diffuse reticulospinal inputs. The diffuse innervation of the reticulospinal tract is suggested to contribute to the flexion synergy, a prominent motor impairment in chronic stroke in which lifting up at the shoulder of the paretic arm results in abnormal coactivation elbow/wrist and finger flexors. Thus, an increase in monoaminergic drive post-stroke may negatively contribute to reaching function. The goal of this preliminary research is to determine the role of descending monoaminergic drive in post-stroke motor control by pharmacologically manipulating norepinephrine supply to spinal motoneurons and measuring resulting reaching function. Three individuals with chronic hemiparetic stroke participated in 1) pre-medication measures of reaching function followed by 2) the administration a single oral dose of 4mg Tizanidine, followed by 3) on-medication measures of reaching function. Tizanidine is a selective noradrenergic alpha-2 (spinal action) and imidazoline (brainstem action) agonist demonstrated to decrease norepinephrine release. Individuals were instructed to ballistically reach towards a virtual target while lifting their paretic upper limb at the shoulder under varying levels of robot assisted limb support. Medication administration resulted in significant increases in reaching distance in conditions when participants had to actively support their paretic arm and significant increases in reaching velocity in all conditions. These preliminary results suggest that Tizanidine reduces the flexion synergy post-stroke, and that monoaminergic drive modulates the gain of the reticulospinal tract in voluntary motor control post-stroke. A supraspinal reduction in monoaminergic drive may reduce the expression of the flexion synergy and improve reaching function for individuals with chronic hemiparetic stroke.

## T49: Repetitive Paired Brain and Spinal Cord Stimulation Strengthen Spared Circuits and Reduce Hyperreflexia after Cervical Spinal Cord Injury

Ajay Pal[1], Aditya Ramamurthy[1], HongGeun Park[1], Thelma Bethea[1], Aldo Garcia-Sandoval[2], Shivakeshavan Ratnadurai-Giridharan[3], Walter Voit[2], Jason Carmel[1]
*[1]Columbia University Medical Center, New York, NY, USA. [2]The University of Texas at Dallas, Richardson, TX, USA. [3]Burke Neurological Institute, White Plains, NY, USA*

Pairs of stimuli engage associative learning mechanisms to change the nervous system. We developed a paired stimulation approach that relies on proper timing of motor cortex and spinal cord stimulation to alter spinal sensorimotor circuits. When pairing is performed repeatedly, there is a lasting and robust increase in cortical and spinal excitability in uninjured rats. The present study tests the efficacy of paired stimulation in rats with spinal cord injury (SCI). We hypothesized that the tissue spared by SCI would enable paired stimulation to augment motor responses but decrease hyperreflexia. Cortical and biceps EMG electrodes were implanted in adult rats, and baseline testing was done a week before SCI. A moderate C4 contusion (200 kdyne) was performed, and thin and softening electrode arrays were inserted over C5-C6. Beginning 11 days after SCI, we tested the effects of repetitive paired stimulation over 10 days. The protocol uses intermittent bursts to deliver 3000 stimuli over 30 minutes every day for 10 days. After this protocol, rats with SCI had large (>150%) augmentation of both cortical and spinal motor evoked potentials (MEPs) that decreased over 2 hours to 50% increase. The magnitude and the duration of the effects were similar in rats with and without SCI, indicating that spared circuits mediate pairing effects. In the group of rats with repetitive stimulation, but not an injury only control group, MEPs increased more than 2-fold over the 10-day stimulation period. The difference between groups was maintained weeks after SCI, indicating a durable change in physiology. In both groups, SCI diminished the rate-dependent decrease in the H-reflex, consistent with hyperreflexia. After 10 days of paired stimulation, rats with stimulation had much less hyperreflexia than injury-only controls. Thus, paired stimulation produces stronger cortical and spinal MEPs, decreased hyperreflexia and the circuits spared after SCI were sufficient to enable long-term plasticity.

Key words:
electrical stimulation; spinal cord injury; paired stimulation; H-reflex; spasticity; neuromodulation.

## T50: Transcranial Direct Current Stimulation Over Lesioned Motor Cortices Reduces the Expression of the Flexion Synergy and Nonlinear Brain-Muscle Connectivity in Hemiparetic Stroke

Yuan Yang, Runfeng Tian, Mark Cummings, Justin Drogos, Julius Dewald
*Northwestern University, Chicago, USA*

A hallmark impairment post-stroke is a loss of independent joint control in the paretic arm resulting in abnormal co-activation of shoulder abductors and arm/hand/finger flexors, clinically known as the flexion synergy. Evidence from previous studies indicates that the flexion synergy is likely caused by an increased abnormal reliance on the non-lesioned cortico-reticulospinal tracts (CRST) after a stroke-induced loss of direct corticofugal projections. Our recent work demonstrated that the expression of the flexion synergy is associated with enhanced nonlinear connectivity between the brain and muscles from the contralesional hemisphere. This is very likely because nonlinear processing of cortical input is cumulatively enhanced when the motor command passes through multiple synaptic connections of the CRST. Recent studies and meta-analysis indicate that non-invasive brain stimulation such as transcranial direct current stimulation (tDCS) can improve the motor function of paretic arm post stroke. However, the neural mechanism underlying its effects is still unknown. We hypothesize that anodal tDCS over lesioned motor cortices improve the arm function via facilitation of residual corticospinal projections and therefore reducing reliance on the CRST. If so, the anodal tDCS should reduce the expression of flexion synergy and nonlinear brain-muscle connectivity (BMC). In this preliminary study, we measured the flexion synergy elbow torques, brain signal (EEG) and muscle activity (EMG) in 3 chronic hemiparetic stroke participants when lifting their paretic arm with 30% of their maximum voluntary shoulder abduction torque before and after 20 min anodal tDCS stimulation over the motor region in the lesioned hemisphere (current density: 0.04 $mA/cm^2$). The nonlinear connectivity between EEG and EMG (i.e., nonlinear BMC) was estimated by using a novel signal processing method that is a nonlinear extension of cortico-muscular coherence method based on high-order spectra. We found that the flexion synergy elbow torque and nonlinear BMC decreased after the tDCS. This result supports our hypothesis and indicates that tDCS has the potential to be combined with physiotherapeutic interventions that aim at reducing the maladaptive usage of the CRST and associated motor impairments post hemiparetic stroke.

## T51: Chronic Stroke Hemispheric Dominance and Task Specific fMRI Laterality of Cortical Motor Activation

David Cunningham[1,2], Alison Rickert[1,2], Ela Plow[3], Jayme Knutson[1,2]
*[1]Case Western Reserve University, Cleveland, USA. [2]MetroHealth Rehabilitation Institute, Cleveland, USA. [3]Cleveland Clinic, Cleveland, USA*

Chronic stroke fMRI studies suggest that greater lateralized activity in the ipsilesional hemisphere during movement of the impaired upper-limb is associated with better motor outcomes, whereas bilateral activation is associated with poorer motor outcomes. These studies help inform therapeutic research interventions that aim to promote motor recovery by increasing the activity of the ipsilesional hemisphere and decreasing the activity of the contralesional hemisphere through methods of non-invasive brain stimulation and forced practice of the impaired upper-limb. But, recovery following these interventions is variable, suggesting that targeting hemispheric laterality may not be the most efficacious approach. Factors that may influence laterality index and its usefulness in predicting motor disability are hand dominance relative to the impaired upper-limb and the task performed during fMRI. Our objective was to explore whether laterality of cortical motor activation can, in part, be explained by hemispheric dominance and task specificity, similar to previous able-bodied studies. Twenty-eight, right handed participants with chronic hemiplegia and 22 age-matched able-bodied participants performed either whole-hand self-paced flexion-extension (non-dominant hemisphere lesion: N = 6; dominant hemispehre lesion: N = 13;  able-bodied controls: N = 12) or whole-hand sinusoidal wave tracking (non-dominant hemisphere lesion: N = 4; dominant hemisphere lesion: N = 5; able-bodied controls: N = 10) of the impaired limb inside the scanner. Group fMRI analysis revealed broad activation patterns within the higher motor, motor, and parietal regions for both tasks and greater laterality during dominant hand tracking. However, overall, there is greater bilateral activation in participants with non-dominant hemisphere lesions during paretic hand self-paced flexion extension and sinusoidal wave tracking, and these results are comparable to non-dominant hand movements within the controls. These results may help explain the variance in recovery following therapies that aim to increase activity in the ipsilesional hemisphere and may offer alternative therapeutic cortical targets dependent on impaired hand dominance and task specificity.

## T52: Soft Robotic Exosuits for Targeted Gait Rehabilitation After Stroke: A Case Study

Franchino Porciuncula[1], Teresa C. Baker[2], Dheepak Arumukhom Revi[1], Jaehyun Bae[1], Regina Sloutsky[2], Lauren Baker[1], Terry Ellis[2], Conor J. Walsh[1], Louis N. Awad[2,1,3]
*[1]Paulson School of Engineering and Applied Sciences, and Wyss Institute for Biologically Inspired Engineering, Cambridge, MA, USA. [2]College of Health and Rehabilitation Sciences, Sargent College, Boston University, Boston, MA, USA.*
*[3]Department of Physical Medicine and Rehabilitation, Harvard Medical School, Cambridge, MA, USA*

### Introduction:
Reduced forward propulsion and foot clearance are pervasive deficits in post-stroke gait that limit post-stroke recovery. Our team has developed a soft robotic exosuit that provides assistive torques in parallel with the paretic ankle plantarflexor and dorsiflexor muscles, showing immediate augmentation of paretic propulsion and foot clearance, a reduced energy cost of walking[1], and increased walking speed and distance[2]. We posit that these immediate benefits can be enhanced by gait training with the device and leveraged to produce gait improvements that persist beyond the use of the device. This preliminary study aimed to assess the rehabilitative effects of an exosuit-augmented gait training program on targeted clinical and biomechanical outcomes.

### Methods:
A 58-year old male with chronic (54 mo) left-sided hemiparesis was enrolled in this case study. Using a crossover design, we administered exosuit-augmented gait training followed by comparable gait training without the exosuit. Each intervention consisted of six sessions of training provided over a 2-week period, separated by a 7-week washout. For both interventions, a physical therapist administered progressive, task-specific, and high-intensity gait training directed at increasing walking speed. To assess the effect on clinical outcomes, the 10-Meter Walk Test and 6-Minute Walk Test were performed before and after each intervention. To assess the effect on biomechanical impairments, evaluations were conducted before and after each intervention on an instrumented treadmill at matched walking speeds. All evaluations were conducted without the exosuit. Examination of pre-to-post changes was based on 95% confidence intervals and paired *t*-tests, with alpha level at 0.05.

### Results:
As hypothesized, exosuit-augmented gait training produced meaningful changes[3] in fast walking speed (pre-post Δ: +0.12 m/s) and walking distance (pre-post Δ: +86 m). In comparison, training without the exosuit resulted in modest increases in fast walking speed (pre-post Δ: +0.04 m/s) and walking distance (pre-post Δ: +37 m). Similarly, exosuit-augmented gait training resulted in increased paretic ankle angle at push-off (+58.78%), stride length (+6.70%), paretic ankle plantarflexion moment (+8.33%), and paretic propulsion (+10.52%) ($p$'s $< 0.05$). In contrast, gait training without the exosuit failed to demonstrate changes in ankle angle at push-off, stride length, and ankle plantarflexion moment ($p > 0.05$). Instead, there was a reduction in forward propulsion (-9.18%) ($p < 0.05$). Taken together, these results demonstrate that exosuit-augmented gait training uniquely retrains a propulsion-based walking strategy not observed after gait training without an exosuit.

### Conclusion:
This case study provides early evidence that targeted gait training with a soft robotic exosuit may deliver improved walking outcomes compared to gait training without an exosuit. The results from this case study encourage further examination in larger samples.

## T53: Understanding Enablers and Barriers to Using Technology with People with Traumatic Brain Injury

Michael Munsell, Emily Dubas, Sadhvi Saxena, Jason Godlove, Swathi Kiran
*The Learning Corp, Newton, USA*

Research has shown that people with neurological disorders experience continued improvement in speech, language, and cognitive skills with ongoing rehabilitation. Despite this, barriers such as insurance coverage and proximity to clinics can hinder a patient's ability to access the therapy required for optimal functional recovery. To offset this lack of sufficient therapy, the use of home-based technology in rehabilitation has become a growing area of research. The use of technology presents its own challenges, however, with engagement tending to be lower among the elderly and those that live in rural areas. This study retrospectively analyzed the data for patients with traumatic brain injury (TBI) that used Constant Therapy (CT), a cloud-based rehabilitation program that delivers standard speech and language therapy exercises via tablet, to determine if usage patterns differed by patient demographic characteristics. User demographics included age, gender, time post-onset, and urban vs. rural geographic location. Activity metrics examined were 1) the total number of completed therapy sessions and 2) the average number of active days per week, both during the first 20 weeks of CT use. The effect of demographic covariates on therapeutic activity was assessed using ANOVA and linear regression. 646 patients with TBI and a language and/or cognitive deficit were included in the analysis, with a mean age of 48.9 years (±18.1), 41.5% female, 8% living in a rural location, and 42.3% having acute condition ( ≤6 months post-onset). The average patient completed 35.4 therapeutic sessions and engaged with the platform 3.1 days per week. ANOVA results suggest a statistically significant effect of gender ($F(1,644)=6.33$, $p<0.05$) and acute condition ($F(1,644)=5.28$, $p<0.05$) on the total number of sessions completed, and no statistically significant effect of any demographic characteristic on the average number of active days per week. After controlling for all model covariates, patients with chronic TBI completed 7.96 more sessions than patients with acute condition ($p<0.05$) and male patients completed 8.44 more sessions than female ($p<0.01$). Results from the linear regression confirmed no statistically significant impact of age, gender, geographic location or acute status on the average number of days per week a patient engaged with the digital platform. Although the average TBI patient in our sample was young and lived in an urban setting, patients that were older or from a rural location did not differ in their use of digital therapy after accounting for gender and time post-TBI onset. Our results suggest that typical barriers to technological adoption may not impact a patient with TBI's ability to engage with home-based rehabilitation technology. However, clinical characteristics such as time post-onset suggest that chronic TBI survivors likely need and are able to access digital rehabilitation.

## T54: Virtual Reality Treatment for Phantom Limb Pain

Elisabetta Ambron[1], Laurel Buxbaum[2], Katherine Kuchenbecker[3], Alexander Miller[4], Branch Coslett[1]
*[1]University of Pennsylvania, Philadelphia, USA. [2]Moss Rehabiltation Research Institute, Elkins Park, USA. [3]Max Planck Institute for Intelligent Systems, Stuttgart, Germany. [4]University of Pennsylvania, Philadelphia*

Up to 90% of amputees experience sensations in their phantom limb, often including strong, persistent phantom limb pain (PLP). Standard treatments do not provide relief for the majority of people who experience PLP, but virtual reality (VR) has shown promise. This proof-of-concept small-scale clinical trial provides additional evidence that game-like training with low-cost immersive VR activities can reduce PLP in transtibial lower-limb amputees. Six participants attended 5-7 sessions in which they experienced a visually immersive experience without leg movements, followed by 10-12 sessions of targeted lower-limb VR treatment (custom games played with leg movements, accompanied by real-time rendering of two intact legs in a head-mounted display). A motion tracking system mounted on the intact and residual limbs controlled the movements of both virtual extremities. All participants except one experienced a significant reduction of pain immediately after each VR session, and their pre-session pain levels also decreased greatly over the course of the study. Additionally, there was preliminary evidence that the targeted lower-limb treatment may be more efficacious than the distractor treatment. The low-cost VR intervention we assessed appears to be a feasible and efficacious treatment of PLP in lower-limb amputees.

## T55: Quantifying Compensatory Trunk Movements During Goal-Directed Arm Reaches in Chronic Stroke Survivors – A pilot study

Bokkyu Kim
*SUNY Upstate Medical University, Syracuse, NY, USA*

Chronic stroke survivors commonly employ compensatory trunk movements during goal-directed arm reaches. Previous kinematic studies have used trunk displacement in the sagittal plane to quantify the compensatory trunk movements during goal-directed arm reaches. However, this measure does not capture compensatory trunk rotation, lateral flexion, and shoulder elevation. This pilot study aims to test the feasibility of shoulder marker trajectory length as a measure of compensatory trunk movements during goal-directed arm reaches in chronic stroke survivors.

### Methods:

We recruited two non-disabled young adults and two chronic stroke survivors with mild upper extremity motor impairment. Each participant performed goal-directed arm reaching and grasping a wood cube (2 X 2 $cm^2$) with a pair of chopsticks. Non-disabled participants performed these tasks with their dominant arm, and chronic stroke survivors performed with more affected arm, which was their dominant arm before the stroke. Participants hold a pair of chopsticks and place tips of chopsticks at home position. Then they were asked to reach and grasp a wood cube located 20 cm in front of the home position. They were provided the sensory-level electrical stimulation on their non-dominant or less-affected arm provided as a cue to initiate arm reaches. They repeated the task 10 times. Positions of thoracic, shoulder, elbow, wrist, hand, and a tip of a chopstick were recorded using a motion capture camera system. We calculated trunk displacement and shoulder trajectory length to quantify the trunk and shoulder compensation during goal-directed arm reaches. Trunk displacement was calculated as $\mathrm{sqrt}((Trunk\_X_k - Trunk\_X_1)^2 + (Trunk\_Y_k - Trunk\_Y_1)^2 + (Trunk\_Z_k - Trunk\_Z_1)^2)$, and Shoulder trajectory length was calculated as $\mathrm{sum}(\mathrm{sqrt}((Shoulder\_X_{t+1} - Shoulder\_X_t)^2 + (Shoulder\_Y_{t+1} - Shoulder\_Y_t)^2 + (Shoulder\_Z_{t+1} - Shoulder\_Z_t)^2))$ from t=1 to t=k, where *X*, *Y*, and *Z* are the positions of the trunk or shoulder marker in x-, y-, and z-axis, respectively; *t* is the time frame; *k* is the maximum time frame at the end of arm reach.

### Results:

There was no significant difference in trunk displacement between non-disabled young adults and chronic stroke survivors. However, stroke survivors showed a greater shoulder marker trajectory length than non-disabled young adults.

### Discussion:

Our preliminary results support that shoulder trajectory length would be a more sensitive measure of compensatory trunk movements than trunk displacement during goal-directed arm reaches in people with chronic stroke. Shoulder trajectory length would be a feasible measure of trunk compensation that captures not only trunk displacement in one axis but also other trunk compensatory movements and shoulder elevation in 3-dimensional space.

## T56: Review of Telerehabilitation for Stroke-related Deficits

Jennifer Mao[1], Kurt Knepley[1], Abhi Jain[1], Noam Harel[2]
*[1]Philadelphia College of Osteopathic Medicine, Philadelphia, USA. [2]Icahn School of Medicine at Mount Sinai, New York, USA*

### Background:
Stroke is the leading cause of serious long-term disability in the US. Barriers to rehabilitation include cost, transportation, and lack of personnel and equipment. Telerehabilitation (TR) has emerged as a promising modality to improve costs, accessibility, and patient independence. TR allows providers to remotely administer therapy via video, potentially increasing access to underserved regions.

### Objectives:
To describe the types of stroke rehabilitation therapy delivered through TR and to evaluate whether TR is as effective as traditional in-person outpatient therapy in improving satisfaction and post-stroke residual deficits such as motor function, speech, and disability.

### Methods:
A literature search of the term “telerehabilitation and stroke” was conducted across three databases. Full-text articles with results pertaining to TR interventions were reviewed.

### Results:
35 articles with 1061 patients were reviewed. Types of TR included speech therapy, virtual reality (VR), robotic, community-based, goal setting, and motor training exercises. Frequently measured outcomes included motor function, speech, disability, and satisfaction. All 35 studies reported improvement from baseline after TR therapy. All 15 controlled studies showed equivalent functional outcomes between TR and traditional therapy. Home-based robotic therapy and VR were less costly than in-person therapy. Patient satisfaction with TR and in-person clinical therapy was similar.

### Conclusions:
TR is less costly and equally as effective as clinic-based rehabilitation at improving functional outcomes in stroke patients. TR produces similar patient satisfaction. TR can be combined with other therapies, including VR, speech, and robotic assistance, or used as an adjuvant to direct in-person care.

## T57: Identifying spasticity and Abnormal Synergy Around the Elbow in Stroke Using Linear System Identification, Preliminary Findings from the ReArm Study

Bram Onneweer[1,2], Levinia L. van der Velden[1,2], Joyce Benner[1], Claudia J. W. Haarman[3], Marij E. Roebroeck[1,2], Gerard M. Ribbers[1,2], Ruud W. Selles[1,2]
[1]Erasmus Medical Centre, Rotterdam, Netherlands. [2]Rijndam Rehabilitation, Rotterdam, Netherlands. [3]Hankamp Rehab, Enschede, Netherlands

### Introduction:

Movement disorders after stroke are the result of highly complex interaction of neuronal and muscular properties, which are generally described in spasticity, abnormal synergy, viscoelastic properties and muscle weakness. To overcome the limitations of clinical assessment tools, robotic devices have been developed to provide more reliable, valid and operator-independent measurements of upper limb function. However, these devices generally quantify only one or two impairments simultaneously. We recently developed a Shoulder Elbow Perturbator (SEP), a single robot device that can identify and quantify these different properties. In this study, we provide preliminary results on quantifying spasticity and abnormal synergy in stroke patients using linear system identification and neuromuscular modeling and compare them to healthy controls.

### Methods:

The hemi-paretic upper limb of 17 stroke patients and the non-dominant upper limb of 17 healthy subjects were fixed into the SEP, a one degree of freedom haptic manipulator which allows for different levels of arm support. Continuous random multisine torque perturbations (0.2-12Hz) were applied to the arm around the elbow at five different arm support levels (100%-0%, with 25% increments). Subjects were asked to perform two repetitions of a relax task, instructed to “do nothing”, at all levels of compensation. Linear system identification and neuromuscular modelling were used to identify the intrinsic and reflexive contributions of the muscles. The hypotheses are that spasticity will affect the reflexive properties of the arm and abnormal synergy affect the intrinsic properties of the arm.

### Results:

Preliminary results show increased velocity-dependent (kv) and position-dependent (kp) reflexive parameters in the patient group (PG: kv: 1,9Nms/rad; kp: 7,8Nm/rad) when compared with the healthy control group (HG: kv: 0,3Nms/rad; kp: 2,5Nm/rad). For the patient group, the parameters increased more with decreasing compensation level (PG: to kv: 7,2Nms/rad; to kp: 13,1Nm/rad, HG: to kv: 1,7Nms/rad; to kp: 8,2Nm/rad). To identify spasticity and synergy we clustered four groups based on clinical outcomes: G1 (n=2): spasticity/synergy; G2 (n=4): spasticity/no-synergy; G3 (n=2): no-spasticity/synergy; G4 (n=9): no-spasticity/no-synergy. The spasticity groups (G1, G2) show higher reflexive parameters over compensation levels (kv: 4 to 12Nsm/rad; kp: 8 to 25Nm/rad). The synergy group (G3) show no effects in the intrinsic parameters. Group G4 show similar behaviour as the healthy controls.

### Conclusion:

This study presents preliminary findings on a Shoulder Elbow Perturbator to objectively quantify impairments in stroke. Our findings show increased reflexive contributions, especially in patients diagnosed with spasticity, suggesting spasticity is an impairment in the reflexive pathways. The increase of the reflexive parameters over decreasing compensation levels and the synergy group showing no effect on the intrinsic parameters could suggest that synergy might also be explained using the reflexive pathways. More research is needed to explain the interaction between spasticity and synergy.

## T58: How Do Accelerometer Variables Reflect Compensatory Upper Limb Movements?

Jessica Barth, Joseph Klasner
*Washington University in St. Louis, Saint Louis, USA*

### Rationale and Purpose:

Within stroke rehabilitation, the differentiation between restoration of normal vs. compensation by alternative movement patterns is an area of high interest. As the use of wearable sensors (e.g. accelerometers) gains acceptance for quantifying UL movement, a potential limitation to wide-spread adoption is their inability to capture compensatory movements. The purpose of this secondary analysis was to characterize how accelerometry variables might reflect upper limb compensatory movement patterns. We hypothesized that quantitative variables from accelerometers speak to important information about movement patterns of the UL.

### Methods:

We conducted a secondary analysis of an existing data set. The dataset includes accelerometer variables from 78 subjects completing assessments and therapy during a dose-response study. Calculated variables included hours of use, use ratio of impaired to unimpaired limb, along with other variables to quantify laterality, intensity, and smoothness of movement. The degree of compensatory behaviors for each participant was quantified by coding videotaped assessments of the Action Research Arm Test (ARAT). Videos were coded by 2-3 trained raters in order to determine compensatory movement scores, where higher scores reflect more compensatory movements. Statistics that are planned include correlations between compensatory movement scores and accelerometer variables. Planned analysis on the full data set will include predictive modeling with machine learning.

### Results:

Preliminary results of 39 individuals post stroke indicate moderate relationships between compensatory movement scores and several accelerometer variables. Use of more compensatory movements was associated with lower intensity movement in the paretic limb ($r = -.30$), lower intensity of bilateral movements ($r = -.48$) and less overall movement variability ($r = -.48$). The full results of the 78 participants will be presented at the meeting.

### Summary and Conclusion:

Preliminary results indicate some accelerometers variables are related to the amount of compensatory movement. Although accelerometers are quantifying amount of movement they also reflect important information about movement patterns of the upper limb.

## T59: Acamprosate Attenuates Unmitigated Alcoholism Following Severe Traumatic Brain Injury Affecting the Bilateral Frontal Cortical Regions

Chichun E. Sun, Claire Flaherty
*Penn State Health Neurology, Hershey, USA*

### Objective:
To pharmacologically manage unmitigated alcohol dependence following severe traumatic brain injury to bilateral frontal cortical regions.

### Background:
Traumatic brain injury (TBI) is a form of non-degenerative acquired brain injury, resulting from an external physical force to the head (e.g., fall) or other mechanisms of displacement of the brain within the skull (e.g., blunt trauma or blast injuries). Executive functioning deficits following trauma related pre-frontal lobe injury often include apathy, declines in judgment (dorsolateral) and ability to adapt behavior in response to unexpected rewards or adversities (orbital frontal).

### Study/Design:
SD is a 40-year-old right handed gentleman who suffered an assault related severe TBI in 2014. He presented for severe apathy in the chronic course, requiring supervision to live independently, work, and limit his alcohol intake. Neurological exam findings were unremarkable. Neuroimaging indicated encephalomalacia in the bilateral dorsolateral/orbital frontal and temporal regions. Neuropsychological assessment indicated intact language, memory and visuospatial skills, while executive functioning deficits were evident for judgment, initiative/motivation/drive, and self-regulation of alcohol dependence which consumed his income to the exclusion of food and housing expenses. Acamprosate was initiated at 333mg x2 tid.

### Results:
Reduction of alcohol intake was achieved following 3 weeks of acamprosate management, with family report of reduction from 6 beers daily to 4, accompanied by reduction of weekend drinking of hard liquor. SD reported diminished compulsion to drink, reliably managing gainful employment as a parking lot attendant.

### Conclusions:
Acamprosate, calcium acetylhomotaurinate, is a synthetic compound with a chemical structure similar to the amino acid neurotransmitter gamma-aminobutyric acid (GABA) and the amino acid neuromodulator taurine. Acamprosate is considered to represent a prototypic neuromodulatory approach in the treatment of alcohol dependence, seeking to restore the disrupted changes in neurobiology resulting from chronic alcohol intake[1]. Our findings extend this heuristic framework to include a potential for acamprosate to stabilize self-regulatory capacities vis a vis alcohol dependence in the chronic course following TBI affecting the bilateral pre-frontal cortical regions.

## T60: Maintaining Written Communication in Nonfluent Progressive Aphasia with Behavioural Therapy and Transcranial Direct Current Stimulation: A case study

Priyanka Shah-Basak[1,2], Alita Fernandez[2], Sabrina Armstrong[2], Monica Lavoie[2,3], Regina Jokel[2,4,5], Jed Meltzer[2,4,6]
*[1]Department of Neurology, Medical College of Wisconsin, Milwaukee, USA. [2]Rotman Research Institute, Baycrest Health Sciences, Toronto, Canada. [3]Toronto Rehabilitation Institute, Toronto, Canada. [4]Department of Speech-Language Pathology, University of Toronto, Toronto, Canada. [5]Department of Psychiatry, Baycrest Health Sciences, Toronto, Canada. [6]Department of Psychology, University of Toronto, Toronto, Canada*

This study presents a case of a 68-year old male (TE) diagnosed with non-fluent variant of primary progressive aphasia (nfvPPA). TE was followed over a period of 1 year (T0, T1). At T0, he presented with deficits in naming, oral repetition and syntax but largely preserved semantics. Agrammatism was also observed but features of speech apraxia appeared unremarkable. At T1, the expressive aspects of language had significantly declined whereby spontaneous speech became non-existent. Significant gray matter shrinkage was localized to the left inferior frontal regions at T1, consistent with nfvPPA pathology. The devastating effects and the rapid decline over the course of a year make this a unique case and calls for specialized treatment alternatives.

Two interventional studies were done in TE: 1) only behavioural therapy at T0, followed by 2) behavioural therapy with transcranial direct current stimulation (tDCS) at T1. At T0, 12 sessions of picture naming therapy (2 sessions/week) were administered. Phonological cues were provided during the first 6 therapy sessions and semantic cues during the next 6 sessions using an errorless learning paradigm. TE attempted to name the pictures both verbally and orthographically. At T1, verbal naming was not possible, so TE wrote his responses. TE received daily sessions of sham-tDCS in the first week and anodal-tDCS (left parietal region; 2mA; 20-minutes/day; 5 days/week) in the second week. During tDCS, both phonological and semantic verbal cues were provided to help improve his word finding and naming difficulties. Resting-state magnetoencephalography (MEG) was collected before and after each week of treatment to assess the treatment-induced neurophysiological changes.

Orthographic results during T1 were evaluated using Levenshtein's distances (LD); a lower LD score indicates greater spelling accuracy. After the first intervention, TE's verbal and orthographic naming appeared to improve more after phonological (*verbal*: M=16; SD=1.6; *orthographic*: M=2.0, SD=3.35) than semantic therapy (*verbal*: M=12, SD=2.53; *orthographic*: M=2.8, SD=5.23; effect size - *verbal*: r=1.57, *orthographic*: r=0.18); differences in effect sizes between verbal and orthographic responses partly stem from preserved orthographic abilities at T0 representing ceiling effects. For the second intervention, orthographic naming abilities improved over the course of anodal-tDCS (M=3.9, SD=0.87) more so than sham-tDCS (M=3.7, SD=0.40. The improvement was maintained at 1-month follow-up after anodal-tDCS. MEG results indicated significantly reduced pathological slow-wave activity (decreased theta and increased beta activity) at and near the site of stimulation.

The case of TE is unique indicating longitudinal trajectory of nfvPPA with severe apraxia. Picture naming therapy with phonological cuing paired with left anodal-tDCS holds promise in improving orthographic naming abilities, despite the observed severity of speech apraxia. The physiological bases of improvement with anodal-tDCS may be related to the induced normalization of neuronal activity.

## F1: Functional Consequences of Upper Extremity Motor Recovery in the First 90 Days after Stroke

***Fletcher H. McDowell Award Finalist**

Kimberly Erler[1], Alison Cloutier[2], Kelly Sloane[2], Joseph Locascio[2], Jessica Ranford[2], Kristin Parlman[2], Nicole Lam[1], Susan Fasoli[1], Teresa Kimberley[1], Seth Finklestein[2], Lee Schwamm[2], Leigh Hochberg[2], David Lin[2]

*[1]MGH Institute of Health Professions, Boston, USA. [2]Massachusetts General Hospital, Boston, USA*

### Background:

There is some evidence suggesting the severity of upper extremity (UE) motor impairment after stroke is associated with activity limitations and participation restrictions; however, there is a limited understanding of how recovery of UE motor function in the first 90 days after stroke comprehensively affects functional outcomes. This study aimed to determine the functional consequences of UE motor recovery in the first 90 days after stroke.

### Methods:

This observational cohort study of adults with arm weakness after ischemic stroke (n=49) included data collected in an inpatient acute stroke care and outpatient ambulatory practice, within a tertiary-care academic hospital in Boston, MA. The Fugl-Meyer Assessment UE (FMA-UE) was the primary predictor of interest for the following functional outcomes: Modified Rankin Scale (mRS), Barthel Index (BI), Stroke Impact Scale-16 (SIS), Patient Health Questionnaire-9 (PHQ-9), PROMIS-Physical Health and PROMIS-Mental Health. Separately for each outcome as the dependent variable, we ran a General Linear Model (GLM) with the predictors of Acute FMA-UE (linear and quadratic terms), 90-day FMA-UE, the interaction of 90-day FMA-UE with Acute FMA-UE (linear and quadratic terms), and the covariate age. The quadratic term for Acute FMA-UE was included because preliminary analyses showed a significant quadratic relation of Acute FMA-UE to 90-day FMA-UE. A backward elimination algorithm was employed for the GLM, with the exception that Acute FMA-UE linear and quadratic terms were always forced in the model.

### Results:

The final backward elimination models showed a significant relationship of 90-day FMA-UE to mRS (partial unstandardized $\beta=-.024$; $p=.003$), BI ($\beta=1.189$; $p<.0001$), SIS ($\beta=.754$; $p<.0001$), and PROMIS Physical Health ($\beta=.134$; $p<.0001$), indicating that the greater the improvement in FMA-UE relative to baseline, the better the 90-day outcome of these metrics. Age was additive to the models for BI ($\beta=-.841$; $p<.001$) and SIS ($\beta=-.418$; $p<.01$), suggesting that older people tended to do worse on these measures. PHQ-9 was significantly negatively correlated with age (Rho = -.378, p=0.0073) but not with Acute or 90-day FMA-UE. Finally, there were no significant predictors in this study of 90-day PROMIS Mental Health.

### Conclusion:

Our findings indicate that there are specific functional consequences of UE motor recovery in the first 90-days post stroke. The greater the improvement in FMA-UE relative to baseline value, the better the outcome on activity-based and motor-weighted participation outcomes. However, the magnitude of UE motor recovery did not impact psychosocial outcomes. Thus, independent of the goal of enhancing motor recovery, comprehensive neurorehabilitation in the first 90 days after stroke should focus on psychosocial aspects of recovery for individuals following stroke.

## F2: The feasibility of Using the Kinarm Exoskeleton for Robotic Stroke Rehabilitation

Alexa Keeling[1,2], Jennifer Semrau[3], Mark Piitz[2], Stephen Bagg[4], Andrew Demchuk[1,2], Janice Eng[5], Nils Forkert[1,2], Bradley Goodyear[1,2], Michael Hill[1,2], Albert Jin[6], Adam Kirton[1,2], Stephen Scott[6], Sean Dukelow[1,2]

*[1]Hotchkiss Brain Institute, University of Calgary, Calgary, Canada. [2]Department of Clinical Neurosciences, University of Calgary, Calgary, Canada. [3]Department of Kinesiology and Applied Physiology, University of Delaware, Newark, USA. [4]Department of Physical Medicine and Rehabilitation, Queen's University, Kingston, Canada. [5]Department of Physical Therapy, University of British Columbia, Vancouver, Canada. [6]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada*

Up to 80% of stroke survivors have upper-extremity deficits which limit the ability to perform activities of daily living. Most of these individuals pursue rehabilitation to help regain independence. A challenge in many places in the world is that patients only receive a small amount of therapy for their upper extremities (~30 movements/day). To overcome this, we developed robotic protocols to increase therapy dose during the sub-acute stroke phase. Robots offer a means of providing therapy without the need for clinical therapists, thereby increasing the potential dose of therapy for patients in environments where staffing levels limit therapy dose.

We use the Kinarm Exoskeleton lab, which allows participants to complete bimanual movements of the arms in the horizontal plane while interacting with an augmented reality display. In the past, the Kinarm has been used exclusively for assessment purposes as it is a sensitive and objective tool for measurement. However, as the Kinarm offers anti-gravity support to the upper extremities, we have recently explored the rehabilitative potential of this exoskeleton in the early phases following stroke. Here, we present the feasibility of using the Kinarm to implement part of a rehabilitation program for sub-acute stroke survivors.

As part of the pilot study for RESTORE (Robot Enhanced Stroke Therapy Optimizes Rehabilitation), 21 participants that were 38.4 days post-stroke (SD = 20.33) were randomly assigned to either the control group (N = 11) or to receive robotic therapy for 10 days (N = 10). All participants received standard of care therapy as well. Robotic therapy consisted of 8 preprogrammed tasks that aimed to retrain sensorimotor function. This included tracing, reaching, and goal-scoring tasks that were bimanual or unimanual and a task that uses intermittent visual-feedback to facilitate proprioceptive recovery.

Subjects completed the following assessments pre- and post- intervention: Fugl-Meyer Assessment of Upper Extremity (FMA UE), Action Research Arm Test (ARAT), and Functional Independence Measure (FIM). There were no significant differences in baseline clinical scores between the groups (ARAT $p = 0.98$; FMA UE $p = 0.78$; FIM $p = 0.34$). Following the intervention, the robotic therapy group had a significantly larger increase in ARAT scores from baseline compared to the control group (Robot: 9.3 ± 3.31, Control: 1.8 ± 1.47, $p = 0.05$). Furthermore, FMA UE scores approached a clinically significant difference of 5-points between the groups (Robot: 7.3 ± 2.06, Control: 2.5 ± 4.74, $p = 0.08$).

Not only did we see improvements on clinical assessments, but the robotic therapy was also tolerated well by the participants and was accompanied by an overall enjoyment of the therapy tasks. Given these results, we propose that future studies examine the Kinarm Exoskeleton as a tool to increase the dose of upper-extremity rehabilitation post-stroke.

F3: Disruption of Direct and Indirect Descending Pathways in Post-Stroke Individuals: Effects of stimulation timing and activation state

Alejandro Lopez, Jiang Xu, Justin Liu, Morgan Trees, Michael Borich, Trisha Kesar
*Emory University, Atlanta, USA*

Both direct and indirect descending cortical pathways that project onto spinal lower motor neurons (LMNs) have important roles in motor control. Stroke causes disruption in descending modulation of spinal circuits that contributes to elevated spinal circuit excitability. However, if and to what extent stroke impacts the excitability of direct and indirect descending cortical pathways remains unclear. Paring sub-threshold transcranial magnetic stimulation (TMS) with peripheral nerve stimulation (PNS) at specific inter-stimulus intervals (ISIs) induces facilitation of the Hoffman's reflex (H-reflex). Short latency facilitation (SLF) of the H-reflex measures the excitability of direct, fast-conducting descending pathways; long-latency facilitation (LLF) measures the excitability of indirect, polysynaptic, slower-conducting descending pathways. Preliminary findings from our lab show a reduction in SLF and LLF post-stroke. The purpose of this ongoing study was to investigate the effects of ISIs and activation state on post-stroke SLF and LLF. To date, as part of this ongoing study, data have been collected on 5 post-stroke individuals >6-months poststroke. Here, results from 3 stroke survivors are reported. Unconditioned H-reflexes were obtained by delivering PNS to the posterior tibial nerve at the intensity that elicited an H-reflex amplitude at 20% Mmax in the soleus muscle. Sub-threshold TMS (90% motor threshold) was delivered to the lesioned hemisphere, with ISIs between PNS and TMS varying from -10 to +50 ms. Comparison of conditioned versus unconditioned H-reflexes at ISIs within the SLF window showed disruption of SLF (%SLF: 90.5 to 99.76%). All 3 stroke survivors showed facilitation in the LLF ISI range (%LLF: 151.97 to 178.9%). Preliminary results also show enhancement of SLF and LLF during the active versus resting motor state. In summary, the loss of SLF post-stroke, shown here at a range of ISIs, indicates disruption of the fast, direct corticospinal pathway. The observation of LLF suggests that indirect, slower-conducting descending pathways, such as the cortico-reticulo-spinal tract, may contribute to post-stroke neuroplasticity, and merit further investigation. Evaluating the influence of functionally relevant conditions such as activation state and posture on the magnitude of SLF and LLF may provide novel insights about the role of descending cortical pathways in post-stroke motor control.

## F5: Demand or Reorganization? Task dependent contralesional motor cortex activation during the early subacute phase of stroke recovery

Kate Revill[1], Deborah Barany[1,2], Alexandra Caliban[1], Isabelle Vernon[1], Samir Belagaje[1], Fadi Nahab[1], Cathrin Buetefisch[1]
*[1]Emory University, Atlanta, USA. [2]University of Georgia, Athens, USA*

Reorganization of primary motor cortex (M1) in the lesioned hemisphere plays a major role in post-stroke motor recovery and is a key target for rehabilitation therapy. Reorganization of M1 in the hemisphere contralateral to the stroke (contralesional M1) may, however, serve as an additional source of cortical reorganization and related recovery. After stroke, there is a general increase in task-related contralesional M1 activation. While the increased activity may indicate cortical reorganization after stroke, it could also be related to increased task demand similar to task demand-dependent activation of ipsilateral M1 in healthy subjects. Here we test whether the contralesional M1 increase in activity is due to cortical reorganization after stroke, reflective of increased task demand, or is a combination of both.

In this study, patients (N = 17, 6M/11F, mean age = 58.3 years) with ischemic stroke affecting M1 output and related hand paresis were scanned 1 month after stroke. Age- and sex- matched healthy controls (N = 24, 8M/16F, mean age = 63.1 years) were also scanned. Participants manipulated an MRI-compatible joystick to move a cursor into a target in one of four possible locations; stroke patients used the affected hand regardless of dominance and controls performed the task with both the dominant and non-dominant hand. Motor demand was manipulated by varying target size (S, M, L, XL) across blocks of movement trials. Electromyographic activity of the extensor carpi ulnaris muscle was monitored to ensure the execution of strictly unilateral hand movements. In both groups, movement accuracy increased and movement time decreased with increasing target size, though stroke patients were less accurate and had longer movement times than healthy control participants. All participants also performed a visually paced hand flexion/extension task with both hands. An ipsilateral (contralesional) M1 region of interest (ROI) was created for each participant by intersecting significant activation from this task with an anatomical M1 mask.

Our preliminary results demonstrate that healthy control participants show activation of ipsilateral M1 during a demanding task, with ROI activation modulated with task demand so that increasing activation is seen with an increased need for movement precision. Activation in ipsilateral (contralesional) M1 is elevated in stroke patients relative to healthy controls during the task, but preliminary analysis indicates that, similar to controls, activation in ipsilateral (contralesional) M1 ROIs increases as target size decreases and the movement task becomes more demanding.

In replication of our previous results, ipsilateral M1 is modulated by task demand in healthy aged subjects. While the overall activity in contralesional M1 was increased in the stroke patients, the activity was modulated by demand. Additional analysis will determine whether the overall increase in contralesional M1 is explained by a shift in the relative demand of the task.

## F6: Is Transcranial Magnetic Stimulation a Reliable Tool for Studying Neurophysiological Changes Associated with Functional Recovery in Individuals with Incomplete Tetraplegia?

Tarun Arora[1], Kelsey Potter-Baker[2,1], Kyle O'Laughlin[1], Xiaofeng Wang[1], Ela B. Plow[1]
*[1]Cleveland Clinic Foundation, Cleveland, USA. [2]University of Texas Rio Grande Valley, Edinburgh, USA*

### Introduction:

Transcranial magnetic stimulation (TMS) is a non-invasive method of probing brain to study neurophysiology in individuals with spinal cord injury (SCI). To ensure that changes in TMS are a true reflection of neurophysiological changes, it is important to test its reliability. Since, reliability may vary between the muscles above and below lesion that are more and less spared by injury, respectively, it is important to compare reliability of these muscles. Two properties of reliability can be studied - agreement i.e. how similar are the test-retest measurements within unchanging individuals, and reliability ($reliability_{MP}$) i.e. how unchanging individuals are relative to others. We determined the agreement and $reliability_{MP}$ of TMS metrics from upper extremity muscles of different impairment levels in individuals with incomplete tetraplegia.

### Methods:

16 individuals [51+12 years (28-68 years) 3F] with chronic incomplete (AIS B:4; AIS C:1; AIS D:11) tetraplegia (C2-C6) participated in the study. We collected TMS metrics from one strong (MRC > 3) and one weak (MRC < 3) muscle in each participant during test and retest visits separated by at most 2-weeks. Evaluated TMS metrics included measures of corticomotor excitability, output, gain, and somatotopy. We calculated agreement properties [Standard Error of Measurement (SEM) and Smallest Detectable Change (SDC)], and $reliability_{MP}$ [Intraclass (ICC) and Concordance (CCC) correlation coefficients].

### Results:

Data were obtained from 19 strong muscles (Biceps = 9; Deltoid = 3; EDC = 2; Triceps = 5) and 13 weak muscles (Biceps = 2; Deltoid = 2, EDC = 3; FDI = 1; Triceps = 5). Overall, measurement error was found to be high. $Reliability_{MP}$ values for strong muscles were greater than weak muscles. For strong muscles, active motor threshold, center of gravity in x-direction and active motor evoked potential amplitude had an excellent (ICC>0.90 and CCC>0.80) $reliability_{MP}$, whereas for weak muscles only active motor threshold had an excellent $reliability_{MP}$. Strong and weak muscles had moderate to good (ICC = 0.50-0.80 and CCC = 0.40-0.80) $reliability_{MP}$ for all other variables except for cortical map volume and recruitment curve slope, which had poor reliability (ICC< 0.50 and CCC< 0.40).

### Conclusion:

High agreement indicates that TMS metrics collected in individuals with tetraplegia have a large inherent measurement noise; therefore, evaluative interpretations based on individual TMS change should be made with caution as a larger change will be required to indicate true change. High $reliability_{MP}$ values suggest individuals with tetraplegia can be distinguished from one another using TMS.

## F7: Unplanned Interruption of Acute Rehabilitation after Stroke

Amanda A. Herrmann[1,2], Gretchen M. Niemioja[3,4], Ella A. Chrenka[5,3], Sally I. Othman[3], Katherine R. Podoll[3], Annika K. Oie[3], Haitham M. Hussein[5,3,4]

*[1]HealthPartners Neuroscience Center, Minneapolis, USA. [2]HealthPartners Institute, St. Paul, USA. [3]HealthPartners Neuroscience Center, St. Paul, USA. [4]Regions Hospital, St. Paul, USA. [5]HealthPartners Institute, Minneapolis, USA*

### Background:

The goal of this project was to identify causes for the unplanned transfer of patients with a stroke from an inpatient rehabilitation facility (IRF) to an acute care hospital setting. A better understanding of the causes will allow us to predict and minimize such incidents.

### Methods:

Data on our patients were exported using Uniform Data System for Medical Rehabilitation, which is a national rehabilitation outcomes measurement program in which our Commission on Accreditation of Rehabilitation Facilities (CARF) accredited IRF participates. We exported patients with a stroke diagnosis who discharged from our IRF to our acute care hospital setting from 2005-2018. We excluded patients who were readmitted for any planned surgery or procedure. Using univariate analysis, this cohort was compared to an age/sex-matched control group of patients with a stroke who were admitted to our acute IRF within the same time frame and successfully completed their rehabilitation stay without transfer.

### Results:

We identified 92 patients with a stroke who had an unplanned transfer from 2005-2018 (age 65 ± 13 years; 38% female; 74% white; 74% ischemic). The control group consisted of 92 age- and sex-matched patients with a stroke diagnosis (75% white; 76% ischemic). The 3 most common indications for transfer were cardiovascular (21%), pulmonary (19%), and other neurological (12%, e.g. hemorrhagic transformation). Compared to the control group, patients with an unplanned transfer had a lower average Functional Independence Measure (FIM) score on admission (9.4 [4.0, 14.8] points lower, *p*-value = 0.001), higher rate of prescribed anti-histamines (17.3% [5.6%, 28.6%] higher, *p*-value = 0.004), anti-psychotics (20.7% [12.6%, 30.1%] higher, *p*-value <0.001), sedatives/hypnotics (44.6% [33.4%, 55.2%] higher, *p*-value <0.001), benzodiazepines (34.8% [24.5%, 45.0%] higher, *p*-value <0.001), and narcotics (37% [24.0%, 48.4%] higher, *p*-value <0.001). For the unplanned transfer group, the median length of stay after transfer to an acute inpatient unit was 5 (3-8) days, after which 41% returned to our acute IRF, 19% passed away, 15% discharged home, and 14% discharged to a skilled nursing facility.

### Conclusion:

The most common causes for transfer from an acute IRF to an acute care hospital setting were cardiopulmonary and neurological. In addition, the majority of patients who transferred did not return back to the acute IRF. Finally, sedatives/hypnotics were higher in the unplanned transfer group, therefore practitioners should be vigilant in patients who are prescribed such medications.

## F9: Does Haptic Feedback Support Motor Learning with a Prosthesis? A neurobehavioral evaluation

***Presidential Award Finalist**

John Johnson, Lewis Wheaton
*Georgia Institute of Technology, Atlanta, USA*

Prosthesis use following an amputation poses a unique challenge partially due to lost motor, structural, and somatosensory function. This is especially true for upper-extremity amputations. Despite technological advances in structural and control systems, prosthesis rejection rates remain high. The question of whether augmented somatosensory feedback, such as vibrotactile feedback, improves motor learning and control during prosthesis use remains open. To further address this question we recruited healthy intact subjects to use a prosthesis (n=10) or a pair of tongs (n=10) to perform a repetitive reach and grasp task. The task involved the use of different size disks to assess the participant's ability to learn efficient reach and grasp strategies as a measure of augmented feedback integration. Prosthesis users were provided vibrotactile feedback indicative of successfully grasping the disk in either the first or second half of their trials, with order randomized. The tongs users served as a control to quantify augmented movement without proprioception at the grasp point and did not receive vibrotactile feedback. High-density electroencephalography (EEG) and motion capture data were collected during the study. Kinematic measures in prosthesis users were not improved by vibrotactile feedback and showed a greatly exaggerated maximum grasp aperture relative to disk size during reach-to-grasp, as well as highly variable grasp begin time, time to peak aperture, and transport velocity. The maximum grasp aperture further increased when vibrotactile feedback was provided. Kinematic effects of prosthesis use compared to tongs use include more variable grasp begin time, time to peak grasp aperture, transport begin time, as well as decreased disk transport velocity with increased variability, and increased time to complete the task. EEG results show an increase in recruitment of parietofrontal networks including premotor and parietal areas in the presence of vibrotactile feedback. Prosthesis use with vibrotactile feedback showed increased parietofrontal activity compared to tongs. Further, vibrotactile feedback did not ameliorate the decreased velocity and increased variability of movements performed during the task as compared to the tongs group or prosthesis use without vibrotactile feedback. Thus, vibrotactile feedback did not facilitate development of a motor program for prosthesis use after short-term practice, was shown to be detrimental to grasp aperture-setting efficiency, and appears to interfere with anticipatory motor learning with a prosthesis.

## F10: Mapping of Motor Responses to Epidural Electrical Stimulation of the Cervical Spinal Cord in Humans Suggests Recruitment of Dorsal Root Afferents and Strong Integration Between Segments

Bushra Yasin[1,2], Steve Karceski[3], Oleg Modik[3], Evgeny Shelkov[3], Michael Virk[2], Jason Carmel[1,4]

*[1]Department of Orthopedic Surgery, Columbia University, New York, USA. [2]Department of Neurosurgery, Weill Cornell Medicine, New York, USA. [3]Department of Neurology, Weill Cornell Medicine, New York, USA. [4]Department of Neurology, Columbia University, New York, USA*

### Abstract:

Spinal cord stimulation can enable some recovery of movement in people with paralysis. Augmenting recruitment of spinal sensorimotor circuits depends critically on the location of the stimulation. A study performed in rats in our lab revealed that stimulating the cervical spinal cord laterally over the dorsal root entry zone produced stronger motor evoked potentials compared to midline stimulation. In contrast, changing the rostral to caudal location within the cervical enlargement did not markedly change the responses in two forelimb muscles. These data suggest a model of activation of afferent axons as they enter the spinal cord, rather than ascending fibers in the dorsal columns, as proposed for models of pain modulation. Given the substantial anatomical differences between rodents and humans, an important gap in our knowledge is whether muscle responses to cervical stimulation will be conserved. We hypothesized that muscle responses to electrical stimulation of the cervical spinal cord in people will be similar to those observed in rats.

### Methods:

To test the hypothesis, we performed epidural electrical stimulation mapping of the cervical spinal in people (n=3) undergoing clinically indicated multi-level laminectomy. A hand-held bipolar electrode was used for epidural stimulation on the dura overlying the cervical enlargement. In each location, we defined the threshold as the lowest stimulation intensity to provoke motor evoked potential (MEP). We also measured the peak-to-peak amplitude of the MEP of the most responsive muscle to a fixed current intensity (120% of threshold). Threshold and MEP amplitude were tested in midline and ~3mm lateral to midline at several locations between C4 and C8.

### Results:

In all 3 patients, lateral stimulation provoked MEPs at a lowest threshold compared to midline stimulation. In addition, MEPs were increased by at least 50% for lateral stimulation over midline. Stimulation of a segment produced MEPs in muscles innervated at that level, as well as other levels of the cervical spinal cord. In addition, leg muscles were often recruited at a stimulus intensity near threshold for provoking arm muscles. Moving the stimulating electrodes across levels usually did not significantly alter the muscles recruited.

### Conclusion:

Muscle responses to dorsal epidural stimulation were far stronger lateral compared to medial. Similar responses at different cervical segments suggest that strong connections between segments, including between the cervical and lumbar spinal enlargements. These results are consistent with our rodent data, suggesting that muscle responses to cervical stimulation are conserved, and that large diameter afferents might be involved in humans as well.

## F11: Spatial Aiming and Far Bias to Predict Functional Disability in Spatial Neglect

A.M. Barrett[1,2,3], Phalgun Nori[2,3], Elizabeth Murray[4], Jenny Masmela[1]
*[1]Kessler Foundation, West Orange, USA. [2]Kessler Institute of Rehabilitation, West Orange, USA. [3]Rutgers New Jersey Medical School, Newark, USA. [4]JFK Neuroscience Institute, Edison, USA*

Although spatial neglect after right brain stroke is known to cause tremendous functional disability, the underlying mechanisms of asymmetric awareness, response and action in this disorder are still unclear. Our program developed a validated method of identifying spatial "Aiming" motor-intentional bias, and separating it from the traditionally-identified deficit in spatial neglect, "Where" perceptual-attentional errors. Spatial "Aiming" bias, which we can quantify with computerized line bisection testing in the laboratory, is a clinical biomarker, independently altered by prism adaptation therapy (PAT), by bromocriptine medication, and predicting good response to PAT.

To learn about the magnitude of spatial Aiming errors in near and far space, and their relationship to functionally-relevant measures of spatial neglect, we tested 11 patients with right brain stroke and spatial neglect on computerized line bisection. We also tested a group of 22, age-matched healthy controls.

Right brain stroke survivors (6 women, mean age 65.5 years) with spatial neglect (Behavioral Inattention Test-conventional subtest or BIT-c, mean score = 92/146) bisected lines in near and far space as part of a computerized task. We used linear regression analysis to investigate predictors of the BIT-c, itself a previously validated predictor of daily life functional disability. We built a regression model with BIT-c as the dependent variable, and near Where (mean 0.5 mm rightward; SD 6.65), near Aiming (mean -6.1 mm; SD 12.23) far Where (mean 4.5 mm, SD 13.20), far Aiming errors (mean 1.6, SD 13.41) and age as possible independent predictors. The model was significant ($F = 6.96$; $p = 0.026$) and explained 75% of BIT-c variance. Near Aiming bias, and far Where and Aiming bias were significant independent predictors of BIT-c ($p < 0.05$) after a Bonferroni correction. Near Where perceptual-attentional asymmetry, the traditionally-identified core symptom of spatial neglect, did not independently predict functionally-relevant BIT-c scores. Near Aiming, Far Where, and Far Aiming errors in stroke survivors with spatial neglect were outside 95% confidence intervals for healthy controls; near Where errors were within the 95% control confidence intervals.

In our subjects with spatial neglect, spatial motor Aiming bias in near and far space, and far Where bias, were potential biomarkers predicting functional disability. Future studies should assess the specific functional impact of Aiming bias and far space errors on functionally-relevant indices. Aiming bias may affect posture, sit-to-stand transfers and balance. Spatial Aiming may be an important outcome measure in future spatial neglect rehabilitation research.

## F12: Towards Quantifying Rehabilitation with Wearable Sensors and Deep Learning

Avinash Parnandi[1], Aakash Kaku[2], Natasha Pandit[1], Carlos Fernandez-Granda[2], Heidi Schambra[1]
[1]*New York University School of Medicine, New York City, USA.* [2]*New York University Center for Data Science, New York City, USA*

### Introduction:

Rehabilitation training after stroke commonly focuses on practicing activities of daily living (ADLs), comprised of functional movements and, more fundamentally, functional primitives. Animal models have demonstrated extensive motor recovery if many functional movements are trained early after stroke. In humans, the optimal rehabilitation dose to maximize recovery is not known, in part because a tool to precisely but pragmatically measure rehabilitation does not currently exist. We are building a measurement tool that can objectively decompose ADLs into their constituent primitives. We report here developments in the first important step of building this tool – the automatic identification of functional primitives that constitute various ADLs.

### Methods:

32 stroke subjects (gender: 18F/14M; paretic side: 14R/18L; age: 56.2 ± 13.54 years; time since stroke: 6.7 ± 7.57 years; mean Fugl-Meyer score: 44.21 ± 14.26) performed a battery of 9 ADLs in an inpatient gym. Participants wore 9 inertial measurement units (IMUs) on their cervical spine, thoracic spine, pelvis, and bilateral hands, forearms, and arms. The IMU system generated linear accelerations, orientations, quaternions, and joint angles at 100 Hz. Human coders used synchronously recorded video to segment each activity into its constituent primitives: *reach*, *transport*, *stabilize*, *reposition*, and *idle*. This segmentation step also assigned primitive labels to the IMU data. Using labeled IMU data, we trained a sequence-to-sequence convolutional neural network (CNN) in 21 subjects and tested it in 11 subjects. Subjects were chosen randomly and were balanced for paretic side. The model had 14 convolutional layers with batch normalization between each layer to reduce the covariate shift. Data windows of 1 s (with a slide of 0.25 s) were fed into the CNN. Using a softmax activation function, the final layer of the CNN generated the probability of the data sample being each primitive. The winning probability was chosen as the label name. To measure the classification accuracy (positive predictive value, PPV) of the approach, we compared the CNN-generated label against the human-generated label for all data windows.

### Results:

Our approach had an average classification accuracy of 64% for identifying the five primitives. Its lowest accuracy was in identifying *reaches* (PPV 37%), which were commonly confused with *transports*. It was moderately accurate in identifying *repositions* (PPV 46%), which were also confused with *transports.* The approach performed well in identifying *idles* (PPV 67%), *stabilizations* (PPV 62%), and *transports* (PPV 60%).

### Discussion:

We present a novel approach for classifying functional primitives embedded in ADLs, an important step toward dose quantitation in rehabilitation. Though classification performance was modest, the approach performs well above chance (PPV 20%), affirming its plausibility for use in stroke patients. Future work will test other deep network architectures and data augmentation techniques to improve classification performance.

## F13: Effect of Visual Distortion on Limb Selections in Virtual Reality System

Jing Wang, Peter Lum, Sang Wook Lee
*Rehabilitation Engineering Research Center-DC (RERC-DC), Catholic University of America, School of Engineering, Biomedical Engineering Department, Washington D.C., USA*

Virtual Reality (VR) systems can affect the perception of the movements of users by providing visual feedback in an immersive environment. Altered visual feedback have a potential to work as intrinsic reinforcement factors to change individuals' decision-making process and behaviors, and further to counteract the learned non-use of the more impaired limb of stroke survivors. The objective of this pilot study is to examine whether virtual amplification of hand movements in VR system can affect the limb selection patterns of healthy subjects in unsupported reaching tasks.

Ten healthy subjects (21.8 ± 1.4 yrs), who are all right-handed (Edinburgh Handedness Inventory score > 0.85), participated in this study. Each subject completed 5 experimental blocks of 100 unsupported reaching trials in an immersive VR system (Oculus Rift; Facebook Technologies, LLC.). In each trial, subjects can use either hand to reach through a cube target appeared at one of the 14 locations in VR, with two height levels (eye/shoulder level) at each of the 7 horizontal angles (0°; ±7°; ±15°; ±30°). Within each block, the target appeared at the ±30° locations on 8 trials, the ±15° on 24 trials, the ±7° locations on 40 trials, and at the center location on 28 trials. The sequence of target locations was randomized. Subjects were asked to move at comfortable speed. After the baseline testing (first block), two levels of virtual amplification of the movements of the right hand, 1.5 times and 2 times, were implemented in the second and fourth blocks. The sequence of two amplifications levels was counter balanced across subjects. The first block served as a baseline and the third and fifth blocks as washout periods, with no virtual distortions implemented. All subjects were blinded to the interventions. The percent of right hand use was used to characterize subjects' hand selections, and one-way within-subjects ANOVA and post hoc comparisons with Bonferroni correction were used to examine the difference of hand selection choices across conditions (SPSS version 25; IBM Corp.) with a significance level of $p<0.05$.

The frequency of the right-hand usage was found to significantly increase under ×1.5 amplification (72.0%±6.0%) from baseline (61.6%±4.3%) ($p = 0.028$), but not under ×2 amplification (65.9%±6.1%). Our findings support our hypothesis that visual amplification of the hand movements could affect the choice of the limb during functional activities. Our results also suggest that the level of amplification should be carefully selected, since the excessive degree of visual amplification of the movement may not be able to encourage the arm use, as observed in the ×2 amplification condition. Virtual reinforcement of the arm/hand movements in VR may have the potential to promote positive change in limb selection process for the stroke population.

## F14: A Feasibility Study on Laryngeal Vibro-tactile Stimulation as a New Treatment for the Voice Disorder Spasmodic Dysphonia

Juergen Konczak[1], Arash Mahnan[1], Sanaz Khosravani[2], Yang Zhang[3], Peter J. Watson[3]
*[1]Human sensorimotor control lab, University of Minnesota, Minneapolis, USA. [2]Harvard Medical School, Boston, USA.*
*[3]Department of Speech-Language-Hearing Sciences, University of Minnesota, Minneapolis, USA*

Spasmodic dysphonia (SD) is a focal dystonia affecting the larynx. It leads to a chocked or strained speech. SD is not responsive to traditional speech therapies. There is no cure for SD. Injection of Botulinum toxin to laryngeal muscles brings temporary voice symptom relief to some patients, but is not well tolerated by all. Proprioceptive deficits are an underlying feature of SD - a finding that opens an avenue for a missing behavioral treatment for the disease. Specifically, vibro-tactile stimulation (VTS) as a non-invasive form of neuromodulation could be the suitable tool, given that it alters afferent signals from the mechanoreceptors in the vibrated muscles and skin.

### Method:
Here, we examined the effect of laryngeal VTS on speech quality and cortical activity in 13 SD participants. The task involved the repeated vocalization of the vowel /a/ while receiving VTS for a total duration of 34 minutes. Cortical activity was monitored concurrently using EEG.

### Results:
In response to VTS, 9 participants (69%) exhibited a reduction of voice breaks and/or a meaningful increase in *smoothed cepstral peak prominence*, an acoustic measure of voice/speech quality. Symptom improvements persisted for 20 minutes past VTS. The application of VTS induced a significant suppression of theta band power over the left somatosensory-motor cortex and a significant rise of gamma rhythm over right somatosensory-motor cortex indicating that VTS reduces.

### Conclusion:
Our results document that a one-time application of laryngeal VTS can effectively reduce the voice symptoms of SD. The suppression of theta band oscillations has been observed in patients with cervical dystonia who apply effective sensory tricks, suggesting that VTS in SD may activate a similar neurophysiological mechanism. Our results promote the development of wearable, non-invasive, voice-activated, user-programmable medical devices that could apply VTS on laryngeal muscles while monitoring its effect on speech production in real-time.

## F15: Effect of Posture and Activation on Transcranial Magnetic Stimulation-evoked Responses in People Post-stroke

Morgan Trees, Jiang Xu, Alejandro Lopez, Trisha Kesar
*Emory University, Atlanta, USA*

### Introduction:

Transcranial magnetic stimulation (TMS) is widely used to measure corticospinal tract excitability. Presence or absence of TMS-evoked motor evoked potentials (MEPs) has been shown to be a valuable prognostic biomarker for predicting stroke motor recovery. An in-depth understanding of how methodological factors such as posture and muscle state influence TMS-evoked responses is necessary for the rigorous and reproducibility of TMS experiments. However, a majority of TMS studies focus on upper limb muscles, leaving a gap regarding our understanding neuroplasticity processes underlying lower limb muscles. Here, we investigated the effect of posture (sitting, standing) and muscle activation state (rest, agonist activation, antagonist activation, coactivation) on TMS-evoked MEPs of lower limb muscles in people post-stroke.

### Methods:

Individuals with chronic post-stroke hemiparesis (N=12, >6-months post-stroke) participated in one experimental session comprising measurement of TMS-evoked MEPs from paretic ankle muscles. Suprathreshold (120% resting motor threshold) single pulse TMS was delivered over the TA hotspot, and MEPs were recorded using surface electromyography sensors attached to the tibialis anterior (TA) and soleus muscles. Data were collected during multiple testing conditions: seated rest, standing rest, standing coactivation, seated with agonist activated, seated with antagonist activated, and seated with agonist-antagonist coactivation.

### Results:

In our preliminary data analyses, stroke survivors showed a significant enhancement of TA MEP amplitude when comparing rest versus coactivation and TA activated. Soleus MEPs showed a significant increase when comparing rest to coactivation, rest versus soleus activated, and sitting versus standing.

### Discussion:

In response to modification of testing posture and activation state of the targeted (agonist) and antagonist muscles, our study showed a significant modulation of TMS-evoked MEPs recorded from the paretic ankle muscles in individuals post-stroke. Comparison of the current results with our previously published normative data from young able-bodied individuals suggests a decrease or loss of modulation of MEPs following stroke, which may have functional implications and merits future study. Modulation of posture and activation state may help increase the probability of eliciting MEPs from lower limb muscles post-stroke. Our findings provide valuable information that can inform the design of TMS experiments focused on lower limb muscles.

## F16: Using Biomarkers of Neuroimaging and Kinematic Measures to Explain the Variability in Stroke

Sandra R. Alouche[1], Melanie C. Baniña[2,3], Timothy K. Lam[4], Kay-Ann Allen[4], Richard Swartz[4], Alexander Thiel[5,6], Mindy F. Levin[2,3], Joyce L. Chen[4,7,8]

*[1]Master's and Doctoral Programs in Physical Therapy, Universidade Cidade de São Paulo, São Paulo, Brazil. [2]Feil/Oberfeld Jewish Rehabilitation Hospital/CRIR Research Centre, Laval, Canada. [3]School of Physical and Occupational Therapy, McGill University, Montreal, Canada. [4]Canadian Partnership for Stroke Recovery, Sunnybrook Research Institute, Toronto, Canada. [5]Lady Davis Institute for Medical Research, and Jewish General Hospital, Montreal, Canada. [6]Department of Neurology and Neurosurgery, McGill University, Montreal, Canada. [7]Faculty of Kinesiology and Physical Education, University of Toronto, Toronto, Canada. [8]Rehabilitation Sciences Institute, University of Toronto, Toronto, Canada*

### Introduction:

Biomarkers enable us to infer the disease state of an individual. Neuroimaging biomarkers, such as injury to the corticospinal tract (CST) and connectivity between motor regions, provide information on the structural and functional integrity of the motor system, respectively. Kinematic biomarkers, such as speed and accuracy of endpoint movements, as well as trunk and joint rotations, during reaching, provide information about movement performance. Kinematic measures of performance correlate with various neuroimaging measures (Buma et al., 2016; Stewart et al., 2017). Our previous work (Subramanian et al., 2010; Lam et al., 2018) separately examined the role of neuroimaging and kinematic biomarkers to explain the variance in motor impairment post-stroke. The aim of this study is to determine the combined influence of both neuroimaging and kinematic biomarkers in explaining the variance in motor impairment post-stroke in the same individuals.

### Methods:

Individuals with chronic stroke (n=18) were recruited from an ongoing double-blind study. Data collected at baseline prior to intervention is reported. Participants completed an assessment of motor impairment (Fugl-Meyer Assessment-Upper Limb, FMA) and underwent MRI. Participants also completed a reaching task where 3D upper limb and trunk kinematics were recorded using the Optotrak motion capture system. We used FSL to analyze the T1-weighted and resting state functional MRI scans. CST injury was determined from the transverse slice of the CST with greatest overlap with the lesion. Resting state connectivity was determined from the temporal correlation of the BOLD signal between left and right primary motor cortex (LM1-RM1 rs-connectivity). An index of performance (IP) was derived from Fitt's Law, which combines information on the speed and accuracy of the endpoint movement. Trunk displacement, shoulder and elbow range of motion were measured.

### Analysis:

Spearman's correlation between all biomarkers was performed. The hierarchical regression analyses applied the most correlated biomarkers and evaluated their influence on the variability of the FMA. The first model included CST Injury. LM1-RM1 rs-connectivity and IP were added as terms in the second and third models, respectively. The $R^2$ change ($\Delta R^2$) value compared whether the addition of a biomarker increased the explained variance in the FMA.

### Results:

The combination of all three biomarkers explained 51% of the variability in the FMA (adjusted $R^2$=0.51, $p$=0.005). CST Injury ($\Delta R^2$=0.25, $p$=0.04) and IP ($\Delta R^2$=0.21, $p$=0.02) significantly contributed to explaining the variability in the FMA, and LM1-RM1 rs-connectivity showed a trend toward significance ($\Delta R^2$=0.14, $p$=0.09). Trunk pitch (r=0.61, $p$=0.009) and yaw (r=0.59, $p$=0.01) were correlated with the neuroimaging biomarkers but were not included in the regression due to the limited sample.

### Conclusion:

An additive effect of both neuroimaging and kinematic biomarkers explains the variance in the FMA. These preliminary results reinforce the importance of using multiple biomarkers to understand motor impairment post-stroke.

## F17: Shoulder Internal and External Rotation Strength During Abduction and Adduction Loading in Chronic Stroke and Controls

Joseph Kopke[1,2,3], Levi Hargrove[3,1,4], Michael Ellis[2]
[1]*Department of Biomedical Engineering, Northwestern University, Evanston, IL, USA.* [2]*Department of Physical Therapy and Human Movement Scienes, Chicago, IL, USA.* [3]*Center for Bionic Medicine, Shirley Ryan AbilityLab, Chicago, IL, USA.* [4]*Department of Physical Medicine & Rehabilitation, Northwestern University, Chicago, IL, USA*

### Purpose:
Upper extremity abnormal torque coupling, also known as synergy or loss of independent joint control, has been quantified at the shoulder, elbow, wrist, and hand in individuals with hemiparetic stroke. However, internal/external rotation about the shoulder has generally been excluded from analyses and is, therefore poorly understood. Clinically, it is important to know if deficits stem from abnormal synergy or weakness so as to determine proper interventions to maximize function.

### Hypothesis:
Internal and external rotation of the shoulder will be impaired as a function of abduction and adduction torque production respectively, reflecting clinically described flexion and extension synergies.

### Subjects:
12 participants (50% female, mean age 60.8±10.3 years) with chronic (> 1 year, mean 16.8±8.3) hemiparetic stroke with moderate to severe motor impairments (Fugl-Meyer assessment 10 to 45, mean 26.9±8.4) and 12 control participants (50% female, mean age 59.1±9.9 years) completed this study.

### Methods:
Participants were required to abduct and adduct at 0%, ± 25%, and ± 50% of their maximum strength with the arm in a standardized position in the horizontal plane located at shoulder height. The participant was asked to adduct or abduct to maintain their arm between a horizontal ceiling and floor (separated by 10cm). Visual feedback was provided on a monitor. Participants were then required to generate maximal isometric external or internal rotation while continuing to keep their arm off the horizontal surfaces. Humeral rotation torques were normalized to their maximum. A linear mixed-effects model was used to analyze the effects of population and loading condition on external rotation torque and a second one was used to analyze the same factors on internal rotation torque.

### Results:
The effect of adduction/abduction load was significant in all populations with internal ($p<0.0001$) and external ($p<0.0001$) rotation strength decreasing or increasing as a function of abduction load respectively. The ability of the paretic arm to produce humeral rotation torque was significantly less than the other groups for both internal ($p<0.0001$) and external ($p<0.0001$) rotation torque across all load levels. The load and arm interaction was not significant ($p=0.83$).

### Discussion/Conclusions:
The anatomical design of the shoulder and the function of the rotator cuff muscles to provide glenohumeral joint stability limits the amount of external and internal rotation that can be accomplished when not abducting or adducting respectively. Since the paretic arm was less able to produce humeral rotation under all load conditions and the interaction of load and arm was not significant, limitations in the independence of humeral rotation after stroke may be a function of weakness more so than the loss of independent joint control.

### Clinical Relevance:
Torque generation (strength), not abnormal torque coupling (synergy), is more important for internal and external rotation function post stroke.

## F18: Losing Your Mind: Understanding demyelination in the brain after SCI

Gisselle Montemayor, Rogelio Meza, Kelsey Baker
*University of Texas Rio Grande Valley, Edinburg, USA*

### Introduction:

Spinal cord injury (SCI) is a debilitating condition that occurs in approximately 17,500 each year in the United States. A growing body of literature has begun to document how initially after SCI, neurodegeneration can occur in the brain as well as the spinal cord. It has been suggested that the additional neurodegeneration in the brain can impact baseline function as well as initial recovery potential in acute phases of SCI. Here, we sought to understand how baseline motor function and recovery potential in chronic SCI patients can be influenced by neurodegeneration in the brain.

### Methods:

Fourteen individuals who had sustained injury to the cervical spinal cord (C2 to C8) were enrolled into our study. As a control, we also studied five healthy subjects. T1-weighted magnetic resonance imaging (MRI) and diffusion weighted imaging of the brain was acquired in all research subjects. Following image acquisition, all subjects received two weeks of tailored rehabilitation that targeted their specific muscle weakness. We evaluated loss of myelin in the cerebral peduncle, pons, and motor cortex for all subjects. Loss of myelin was determined for both hemispheres of the brain. We then used regression analysis to understand the relationship between demyelination in the brain and baseline function, as well as, recovery rates of subjects after rehabilitation. All statistical analysis was completed using SPSS, where $p<0.05$ was defined as significant.

### Results:

We observed a wide range of demyelination within the brain in subjects with SCI. Initial analysis suggested that there was significant demyelination in the subcortical regions of the brain (cerebral peduncle and internal capsule) after SCI in comparison to healthy controls (0.61 vs. 0.53; $p<0.05$). Interestingly, we found that the right hemisphere of the brain demonstrated more demyelination compared to the left hemisphere. Changes in white matter in the brain were found to be positively correlated with recovery potential. Specifically, we observed that subjects with more demyelination had less recovery of muscle strength in muscles innervated caudal to the spinal cord injury ($r=0.66$; $p=0.05$). Suggesting that individuals with more demyelination in the brain may not show as much of a direct benefit from traditional rehabilitation approaches.

### Conclusion:

We have observed an association between baseline UEMS and the amount of demyelination in SCI. Our future work will evaluate how changes in myelination in the brain and spinal cord are related and how they influence functional recovery.

## F20: White matter Integrity of Medial Reticulospinal Tract is Increased Post Hemiparetic Stroke

**2019 Fletcher H. McDowell Award Recipient*

Haleh Karbasforoushan[1], Julien Cohen-Adad[2], Julius Dewald[1]

*[1]Northwestern University, Chicago, USA. [2]Polytechnique Montréal, Montréal, Montreal, Canada*

Numerous functional neuroimaging studies of stroke have reported increased neural activity in motor cortices of both lesioned and non-lesioned hemispheres during hand/arm movement. They have also reported that the more severe the impairment, the greater the activity in the contralesional hemisphere compared to the ipsilesional (i.e. a shift of activity to non-lesioned hemisphere). However, it is still unclear what descending motor pathway allows the contralesional motor cortex to control the ipsilateral paretic arm, although one proposed idea suggests brainstem ipsilaterally projecting motor pathways (i.e. reticulospinal or vestibulospinal tracts) may play this role. One reason for this lack of knowledge is that the previous studies have only investigated morphological changes in the brain, where the majority of descending and ascending brain pathways overlap, while these pathways only delineate from each other in the brainstem. Moreover, these pathways continue passing through separate regions in the spinal cord. The goal of this study was therefore to use high resolution anatomical MRI and DTI of both brainstem and cervical spinal cord, as well as novel analysis approaches, to identify altered sensorimotor pathways post chronic stroke. Thirty-six individuals with chronic (>1yr) unilateral subcortical stroke and 31 age-matched controls were recruited to this study. The MRI scans were collected on a 3T Siemens Prisma magnetic resonance scanner. High resolution T1-weighted anatomical and diffusion weighed images were obtained from brainstem and cervical spinal cord. Brainstem diffusion weighted images were acquired using spin-echo echo-planer imaging with the following parameters: TR = 3620 ms; TE = 68.40 ms; FOV = 222 x 222 $mm^2$; voxel size = 1.5 mm isotropic; number of slices = 108. Cervical spinal cord DWI scans were collected with in-plane resolution = 0.8 x 0.8, TR = ~ 600 ms, TE = 61 ms, slice thickness = 5 mm, FOV = 86 $mm^2$, number of slices = 15, b-value = 1000 in 30 directions. Voxel-wise statistical analysis of the brainstem DTI data was carried out using Tract-Based Spatial Statistics in FSL, and spinal cord data preprocessing and analysis was done using spinal cord toolbox version 3.2.2. Our results indicate a significant decrease of white matter integrity in corticospinal tract, lateral and medial reticulospinal tracts, descending medial longitudinal fasciculus, tectospinal tract and cuneate and gracile fasciculi related to the lesioned hemisphere. Furthermore, the results from brainstem and cervical spinal cord DTI analyses indicate a significant increase in the white matter integrity of medial reticulospinal tract at the side of contralesional hemisphere which projects ipsilaterally to the paretic (contralesional) limbs. The decreased white matter integrity of ipsi-lesional corticospinal tract and increased white matter integrity of contra-lesional medial reticulospinal tract are correlated with upper limb motor impairment severity in individuals with hemiparetic stroke.

## F22: Minor Stroke, Serious Problems: The impact on balance and gait capacity, fall rate, and physical activity

Vivian Weerdesteyn[1,2], Jolanda Roelofs[1], Ingrid Schut[3], Anouk Huisinga[4], Alfred Schouten[3,5], Henk Hendricks[6], Frank-Erik De Leeuw[7], Leo Aerden[8], Hans Bussmann[9], Alexander Geurts[1]

*[1]Department of Rehabilitation, Donders Institute for Brain, Cognition and Behaviour, Radboud university medical center, Nijmegen, Netherlands. [2]Sint Maartenskliniek Research, Nijmegen, Netherlands. [3]Department of Biomechanical Engineering, Delft University of Technology, Delft, Netherlands. [4]Rehabilitation Centre Klimmendaal, Arnhem, Netherlands. [5]Department of Biomechanical Engineering, Technical Medical Centre, University of Twente, Enschede, Netherlands. [6]Department of Rehabilitation Medicine, Rijnstate Hospital, Arnhem, Netherlands. [7]Department of Neurology, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, Netherlands. [8]Department of Neurology, Reinier de Graafgasthuis, Delft, Netherlands. [9]Department of Rehabilitation Medicine, Erasmus University Medical Center, Rotterdam, Netherlands*

### Importance:
Recent findings suggest that even after minor stroke persistent balance problems may occur (Batchelor et al., 2015). This notion deserves further investigation, because poor balance is a risk factor for falls and reduced activity levels.

### Objective:
To test the hypothesis that people with minor stroke show persistent balance and gait problems, elevated fall risk, and decreased physical activity levels compared to healthy persons.

### Design:
Longitudinal observational cohort study with 6-month follow-up period.

### *Setting:*
General hospitals and community in the Netherlands.

### Participants:
Participants were included if they had sustained a unilateral supratentorial transient ischemic attack (TIA) or stroke longer than 6 months ago that resulted in motor and/or sensory loss in the contralesional leg. They needed to have shown (near-)complete motor recovery as indicated by a score ≥24 points on the Fugl-Meyer Assessment – Lower Extremity (FMA-LE; range: 0-28).

### Outcome measures:
Mini-Balance Evaluation Systems Test (mini-BESTest), Timed Up and Go test (TUG), 10-Meter Walking Test (10-MWT), 6-item short version of Activity-specific Balance Confidence scale (6-ABC), fall rate, daily physical activity (total time and intensity).

### Results:
245 eligible persons with stroke and 88 healthy individuals were screened for eligibility. Of these, 64 participants with minor stroke (mean age: 63.8yrs) and 50 healthy age-matched controls (mean age: 63.6yrs) were included. Thirty-six participants with minor stroke (56%) showed full leg motor recovery (FMA-LE: 28 and Motricity Index – Lower Extremity: 100). Compared to controls, participants with minor stroke scored significantly lower on the mini-BESTest (24.2±2.3 vs. 26.1±2.1 points), were slower on the TUG (10.0±2.0 vs. 8.6±1.1 seconds), had lower walking speed (1.31±0.22 vs. 1.45±0.16 m/s), and lower 6-ABC scores (79±19 vs. 89±10%) (all $p \leq 0.001$). All statistical differences persisted in the subgroup of full recoverers. Participants with minor stroke fell more than twice as often as healthy individuals (1.1 vs. 0.52 falls per person-year, $p=0.023$). No between-group differences were found for total time of physical activity ($p=0.499$), but intensity of physical activity was 6% lower in participants with minor stroke ($p=0.030$).

### Conclusions:
Individuals in the chronic phase after minor stroke with (near-)complete clinical motor recovery of the paretic leg may still demonstrate deficiencies in balance and gait capacities, a relatively high fall frequency, and lower intensities of physical activity. These results may point at an unmet clinical need in this population.

## F23: Does Transcranial Direct Current Stimulation Improve Reaction Times of People After Stroke During Balance Perturbations, Gait Initiation, or Voluntary Ankle Dorsiflexion Movement?

Milou Coppens[1], Wouter Staring[1], Alexander Geurts[1], Vivian Weerdesteyn[1,2]
*[1]Department of Rehabilitation, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, Netherlands. [2]Sint Maartenskliniek Research, Nijmegen, Netherlands*

### Background and aim:

Non-invasive brain stimulation techniques may enhance rehabilitation in people after stroke, however, current evidence for balance and gait recovery is inconsistent. Transcranial direct current stimulation (tDCS) has been reported to improve hand reaction times (RT) in people with stroke [1]. Therefore, we aimed to investigate whether tDCS would also have a beneficial effect on delayed leg motor responses after stroke. We studied the effect of tDCS on tibialis anterior (TA) RT in three tasks: gait initiation, backward balance perturbations, and voluntary ankle-dorsiflexion movements.
We hypothesized that ipsilesional anodal tDCS 9a-tDCS) would enhance cortical excitability of the affected hemisphere, whereas contralesional cathodal tDCS (c-tDCS) would decrease interhemispheric inhibition of the affected hemisphere, both improving reaction times.

### Methods:

Thirteen participants with chronic supratentorial stroke completed three sessions of 15 min ipsilesional anodal, contralesional cathodal, or sham stimulation (2mA) over the primary motor cortex on separate days. The order of conditions was balanced across participants. In response to a visual cue, participants performed 12 trials of gait initiation with the preferred leg and 12 trials of paretic ankle-dorsiflexion movements as fast as possible while sitting. In addition, participants were subjected to 12 trials of translational support-surface perturbations inducing a backward fall, which they had to overcome with a feet-in-place response. We recorded EMG from the paretic TA and 3D movements of markers on the feet and vertebra C7.

### Results:

On group level, TA RTs did not differ between tDCS conditions in any of the three tasks (Gait: $p=0.690$, Balance: $p=0.239$, Ankle: $p=0.287$), nor were step onsets during gait initiation influenced by tDCS ($p=0.071$). However, C7 displacements following balance perturbations were slightly larger (4mm) after a-tDCS (tDCS: $p=0.027$; a-tDCS vs. sham: $p=0.020$). For gait initiation and balance perturbations, differences between sham and stimulation (a-tDCS or c-tDCS) did not correlate with leg motor impairment. Yet, during ankle dorsiflexion RT differences between c-tDCS and sham were strongly associated with Fugl-Meyer Lower Extremity scores, with more severely impaired patients exhibiting delayed paretic RT following c-tDCS ($\rho=.779$, $p<0.01$).

### Conclusion:

Contrary to our expectations, we found no evidence of tDCS-induced benefits. Interestingly, we found that c-tDCS may even have an unfavourable effect on voluntary leg motor control of the paretic leg in more severely impaired chronic stroke patients. This finding points at potential vicarious control from the unaffected hemisphere to the paretic leg. In addition, the absence of a tDCS-induced effect on gait and balance suggests that such motor behaviour is controlled differently, and inadequately stimulated by our current methods.

## F24: Adaptive Arm Training for Children with Hemiparesis (One-Sided Weakness) as a Result of Acquired Brain Injury (ABI)

Talita Campos[1,2], Kathleen Friel[1,2]
*[1]Burke Neurological Institute, White Plains, NY, USA. [2]Blythedale Children's Hospital, Valhalla, NY, USA*

Bimanual training has been shown to lead to greater gains in arm function compared with practice with the paretic (affected) arm alone.[1-5] An advantage of this approach is that it can be used in individuals with severe paresis.[3,4]

### Aim 1:

Provide limb training in children with hemiplegia from cerebral palsy and/or ABI using a bimanual-to unimanual training approach. We hypothesize that child-friendly upper limb bimanual-to-unimanual training will lead to improved motor outcomes on the Assisting Hand Assessment (AHA), Jebsen-Taylor Test of Hand Function (JTTHF), and Box and Blocks test (BBT).[4]

### Aim 2:

Improve the understanding of the pattern of recovery of isolated joint movements in the pediatric population with hemiplegia following CP/ABI. We hypothesize that individuals receiving device-based bimanual-to-unimanual training will show improvement in active range of motion across upper limb joints.[4]

This study is taking place as part of the Burke-Blythedale Pediatric Neuroscience Research Collaboration in Westchester, NY. Children (n=8, 5 males, 3 females, age 5-17 years) with hemiparesis as a result of ABI participated in a pilot feasibility study that utilizes a robotic device developed at NYU Rusk called the Bimanual Arm Trainer (BAT, *Mirrored Motion Works*, NC)[4]. This device employs mirrored motion, combines motivational features with modern technology and a therapeutic method that links the movement of the arms to retrain a patient's brain. The device provides bimanual-to-unimanual training of simultaneous shoulder external rotation and elbow extension, and independent training of pronation, supination and grasp and release of each hand. Range of motion and speed are recorded during training and feedback and motivation are provided through age-appropriate gaming modules.

Preliminary analysis of the primary outcome measures has shown that bimanual hand and arm use has improved (AHA, $p<0.01$), skill of the affected upper limb (BBT; $p<0.05$), and hand dexterity (JTTHF; $p<0.05$) have also significantly improved. These results are favorable but further study is needed (and ongoing).

## F25: Electrode Montage and Dose of Non-invasive Stimulation – Important considerations for Stroke Recovery applications

Anant Shinde[1,2], David Alsop[1,2], Gottfried Schlaug[1,2]
*[1]Harvard Medical School, Boston, USA. [2]Beth Israel Deaconess Medical Center, Boston, USA*

Reports have shown that transcranial direct current stimulation (tDCS) can modulate cortical excitability in targeted brain regions depending on polarity. Several non-invasive stimulation approaches have been tried to enhance plasticity in the recovery period. Our aim was to determine whether variations in dose and montage of tDCS leads to local and remote changes in regional cerebral blood flow (rCBF) and differential effects in a finger sequence motor learning experiment.

For the motor sequence learning experiment as well as for the imaging studies, we used three different dose levels (Sham, 2mA, and 4mA) and two different electrode montages (unihemispheric or bihemispheric). In both montages, the anodal electrode was placed over the right motor region (C4) while the cathodal electrode was either placed over a left supraorbital region (unihemispheric montage) or over the left motor region (C3; bihemispheric montage). Brain blood flow was examined by applying tDCS within the MRI environment and by obtaining non-invasive arterial blood flow images (ASL) before, during, and after an 8-minute stimulation session. In the finger sequence learning task, subjects were asked to type a randomly chosen sequence of 7 items (using numbers 2-5 on a computer keyboard) with digits 2-5 of each hand several times before and immediately after the 10 min stimulation. The number of correct sequences typed by a participant was counted before and after stimulation, and the percentage change in the correct number of sequences is calculated.

After unihemispheric stimulation, both left and right hand showed improvement in the motor task performance with a clear linear trend for the main effect of dose. Bi-hemispheric 2mA and 4 mA stimulation showed improvements in performance for the left as well as right hand; improvements for the left hand (targeted by the anodal stimulation to the right motor region) was more than the improvements of the right-hand performance.

A significant difference ($p<0.05$unc) in cerebral blood flow between ON and OFF conditions was seen in the peri-rolandic region on the right (targeted with anodal stimulation) showing a linear increase in rCBF between sham, 2mA, and 4mA. Bihemispheric stimulations caused significant changes ($p<0.05$ unc) in blood flow under both anode and cathode electrode for the 2mA and 4mA condition, with the 4mA condition leading to blood flow changes in other connected regions such as the frontomesial region, when the 4mA condition was directly contrasted with the 2mA condition.

Thus, increasing dose of tDCS (up to 4mA) has local (under the electrode) as well as remote CBF effects which can serve as a surrogate marker of variations in tDCS variables. Our analysis so far suggests a linear relationship between tDCS dose and brain/behavioral effects.

## F26: Vagus Nerve Stimulation Paired with Rehabilitation for Upper Limb Recovery After Stroke: 1-year follow up

Teresa Kimberley[1], Navzer Engineer[2], Cecilia Prudente[2], David Pierce[2], Gerard Francisco[3], Nuray Yozbatiran[3], Brent Tarver[2], Reema Casavant[2], Danielle Kline[1], Ann Van de Winckel[4], Jesse Dawson[5]
*[1]MGH Institute of Health Professions, Boston, USA. [2]Microtransponder, Austin, USA. [3]University of Texas Health Science Center at Houston, Houston, USA. [4]University of Minnesota, Minneapolis, USA. [5]University of Glasgow, Glasgow, United Kingdom*

Seventeen participants with chronic ischemic stroke and moderate to severe upper limb impairment were enrolled in a randomized, sham-controlled pilot study to evaluate the safety, feasibility and potential efficacy of Vagus Nerve Stimulation (VNS) paired with rehabilitation for upper limb motor recovery. All participants were implanted with a VNS device and then randomized to Active VNS (n=8; rehabilitation paired with VNS) or Control VNS (n=9; rehabilitation without VNS). Participants in both groups received 6-weeks in-clinic rehabilitation, followed by therapist-prescribed, individualized, daily, 30-min, home exercise program with self-triggered VNS. As previously reported, the average Fugl-Meyer Upper Extremity (FMA-UE) increased by 9.5 points from baseline with Active VNS compared to 3.8 points in Control VNS group (difference, 5.7 points; CI, −1.4 to 11.5; p=0.055) at 3 months. After the 3-month follow-up from the randomized portion of the study, the Control VNS group crossed-over to receive 6-weeks of rehabilitation with Active VNS. Participants in both groups continued their home exercise program with self-triggered VNS for 1 year with additional long-term testing. Here, we report 1-year follow-up results from the pilot study.

Regarding safety and feasibility, there were no VNS treatment-related serious adverse events during the long-term. Stimulation-related adverse events were mild and events possibly related to stimulation included hoarseness and hiccups. No subject withdrew due to adverse events. Two Control VNS subjects discontinued prior to receiving the full crossover VNS. One subject had substantial benefit from rehab-only while the second subject lived a significant distance from the site and decided to drop out to avoid continued travel.

One year after starting home-based therapy, the average Fugl Meyer upper extremity (FM-UE) score for the Active VNS group improved by 10.8 points (n= 8, CI, 4.49, 17.26, p=0.005) from initial baseline. FMA-UE in the VNS Control group, after cross-crossover to VNS, improved by 7.2 points (n=7, CI, -0.9, 15.5, p=0.07) from initial baseline. On average, at one year, 11/15 participants (73%) showed a clinically meaningful improvement in FMA-UE (≥ 6-point change) after receiving Active VNS.

VNS combined with rehabilitation provides long-term benefits to individuals with chronic stroke and warrants further investigation.

F27: Assessing the Structural and Functional Impact of Cerebral Microinfarction in Mice

Melissa Filadelfi, Greg Silasi
*University of Ottawa, Ottawa, Canada*

Microinfarcts are classified as a subtype of ischemic stroke that results in microscopic lesions throughout the brain, ranging from 0.05 to 3 mm in diameter. Within the ageing population (>65 years old), microinfarction is present in ~30% of individuals, whereas this incidence is doubled in patients with vascular dementia. Animal models are needed to better understand the structural and functional consequences of microinfarction.

In our current experiment we employ an intravascular microsphere injection model to quantify and localize ischemic damage globally throughout the brain following diffuse microinfarction in mice. Specifically, mice were surgically injected with ~2000 green fluorescent microspheres (20 µm in size) through the internal carotid artery (ICA) and brain tissue was harvested 1, 3, 7, 14 or 21 days post-stroke to characterize the timecourse of ischemic damage. Prior to perfusion, Evans blue (EB) dye was intravenously injected through the tail vein to label sites with a disrupted blood brain barrier. Brains were removed, sectioned at 50 µm and imaged to visualize the EB label and the fluorescent microspheres.

There was a significant increase in EB dye intensity within the left hemisphere at both 1 ($p=<0.0001$) and 3 days ($p=0.0002$) post-stroke, however subsequent timepoints did not show a significant difference between the injured and intact hemispheres.

Our data indicates that microinfarction produces blood-brain barrier breakdown during the first week after stroke. Our ongoing analyses are further characterizing the histological damage at individual occlusion sites.

## F29: Hypoxic ventilatory response (HVR) and Burst-to-burst Variability in Spontaneously Breathing Urethane-anesthetized Adult Female Rats with Mid-thoracic Moderate Contusion SCI

Christine Wang, William F Collins, Irene C Solomon
*Stony Brook University, Stony Brook, USA*

Spinal cord injury (SCI) at either the cervical or thoracic level can lead to inefficient ventilation by disrupting descending inputs to respiratory motoneurons resulting in altered mechanics of breathing and a reduced ability to adequately and appropriately respond to ventilatory complications. Under these conditions, individuals with SCI may experience bouts of acute hypoxia that vary in severity and/or duration. Recently, the use of acute intermittent hypoxia (AIH) has been proposed as a potential therapeutic intervention to induce spinal motor plasticity and improve respiratory motor function following incomplete cervical ($C_2$) SCI in both rodents and humans; however, much less is known about the effects of hypoxia on respiratory motor output following mid-thoracic SCI, which spares phrenic motoneurons. To begin to address this issue, we examined the effects of a single hypoxic exposure on diaphragm EMG bursts in spontaneously breathing urethane-anesthetized adult female Sprague-Dawley rats 4-weeks after mid-thoracic moderate contusion (200 kdyn) SCI (n=6); both naïve (n=5) and 4-week post SHAM SCI surgery (n=4) rats served as controls. EMG burst frequency and amplitude were measured and quantified at 15-min intervals under baseline (BL) normoxic conditions, at 5-min intervals during hypoxic exposure (12% $O_2$; 15-min), and at 5-min or 15-min intervals during normoxic recovery (up to 60 min). In addition, burst-to-burst frequency and amplitude variability were determined using coefficient of variation (CV) and Poincaré plot analyses from 300 consecutive EMG bursts. For the hypoxic ventilatory response (HVR), we found that both SCI and control rats exhibited an increase in burst frequency (by ~20% and 30% over BL levels, respectively) in response to hypoxia although a variable magnitude decline from peak frequency was noted as the hypoxic exposure progressed. The effects on amplitude, however, were highly variable, resulting in negligible steady-state effects, albeit some SCI and control rats exhibited comparable increases or decreases in hypoxia-induced amplitude changes. Upon return to normoxia, post hypoxic frequency decline of ~15% (below BL levels) was noted in both SCI and control rats, with a return to BL frequencies typically occurring by the 30- or 45-min recovery time point. CV analyses revealed that compared to control rats, SCI rats exhibited slightly lower variability in BL burst frequency and amplitude, and while both CV values increased during hypoxia, the increase in CV for HVR amplitude was not as great as that seen in control rats. Poincaré plot analyses confirmed reduced burst-to-burst frequency and amplitude variability in SCI rats under BL and HVR conditions and revealed that the increases in short-term (SD1) burst-to-burst frequency variability and long-term (SD2) burst-to-burst amplitude variability were attenuated. These data demonstrate that while rats with mid-thoracic contusion SCI exhibit an HVR, the respiratory dynamics of the HVR behaviors exhibit reduced short-term and long-term burst-to-burst variability.

F30: The Relationship between Hand Function and Posterior Parietal Cortex and Primary Motor Cortex Connectivity during Post-Stroke Recovery

Lauren Edwards, Ashley Mangin, Scott Shaeffer, Jacqueline Palmer, Michael Borich, Cathrin Buetefisch
*Emory University, Atlanta, USA*

Our long-term goal is to have a better understanding of the post-stroke neurophysiology that may be contributing to the impairment of skilled hand movements after stroke. Most stroke survivors have a limited ability to perform skilled hand movements, which negatively affects their quality of life. Both the primary motor cortex (M1) and posterior parietal cortex (PPC) play integral roles in sensorimotor integration required for goal-directed voluntary hand movements. Structural and functional connectivity between cortical regions can be modified by stroke across the continuum of recovery. Local and distributed connectivity between M1 and other brain regions has been shown to be reduced acutely with more normal levels observed in the chronic phase of recovery. However, PPC-M1 connectivity post-stroke has not been previously evaluated. Connectivity changes can also parallel recovery of hand motor function, which has the greatest improvement in impairment within the first three months after stroke. The objective of the present study is to test the relationship between PPC-M1 connectivity and paretic hand motor function during the subacute and chronic recovery phases post-stroke. We hypothesize that PPC-M1 connectivity in the affected hemisphere will be decreased in the subacute phase relative to the chronic phase and that increased connectivity will be positively correlated with better paretic hand motor function. In a cross-sectional study design, preliminary data acquisition and analysis was performed on eight patients (5 males, age 61 ± 3.7 years, time post-stroke of 25 ± 10.5 days) during the subacute phase and three patients (2 males, age 58 ± 2.6 years, time post-stroke of 180 ± 7.2 days) during the chronic phase of stroke recovery. Paretic hand motor function was quantified using the Jebsen-Taylor Hand Function Test (JHFT). Cortical activity was measured using 64-channel electroencephalography (EEG) recordings with active electrodes and stored for offline analysis. To evaluate PPC-M1 connectivity, custom MATLAB functions were used to extract imaginary phase coherence (IPC) values within the beta frequency range (15-30Hz) between electrodes overlaying M1 (C3 or C4) and PPC (P3 or P4) of the affected and non-affected hemispheres. IPC values were then correlated with the JHFT scores for the corresponding affected and non-affected hands separately. Our preliminary results suggest there may be no difference in PPC-M1 connectivity between the subacute and chronic phases post-stroke. Although clear correlations between PPC-M1 connectivity and JHFT performance were not observed in the subacute stroke group, there appeared to be a trend for a positive relationship between PPC-M1 connectivity and paretic hand function in the chronic stroke group. Evaluation of additional data will further probe these relationships, while also extending analysis to evaluate differences dependent upon hemisphere of stroke and the level of skillfulness of hand function.

## F31: The Impact of AFO-use on Fall Outcomes and Compensatory Stepping Response of Stroke Survivors During Trip-like Treadmill Perturbations

Masood Nevisipour, Claire Honeycutt
*Arizona State University, Tempe, USA*

Ankle-foot-orthoses (AFOs) are commonly prescribed to treat foot-drop. AFOs enhance walking speed, static balance, mobility, and increase foot clearance during walking which helps prevent stumbles and falls. However, AFO's impact on fall outcomes of stroke survivors is not well evaluated. One study shows AFO-users are at high fall risk (Bethoux et al., 2015). Our objective was to evaluate and compare AFO-users' response during a laboratory-induced trip to clinically matched Non-users to determine what biomechanical properties of AFO-users' response might lead to a fall. Moreover, AFO-users were tested without their AFO to establish how effective the AFO is at assisting the compensatory stepping response required to prevent a fall.

Fourteen AFO-users and eighteen Non-users (age, height, weight, and clinically matched) were exposed to treadmill perturbations that mimic over-ground trips (Owings et al., 2001) while fitted in a safety harness. Fall outcomes, trunk kinematics, step length, dynamic stability, reaction time, and step duration were calculated during the first compensatory step. AFO-users completed the study with and without their AFO. Subjects performed clinical balance and mobility tests including BBS, 10m walk test (comfortable/fast), and TUG.

AFO-users fell 2.2 times more often than Non-users (37.2% vs. 16.9%, $p=0.018$) while the aforementioned clinical scores were the same between the groups (all: $p>0.05$). Trunk flexion and velocity at step initiation and completion were larger for AFO-users compared to Non-users (all: $p<0.003$). Other measures were not different between the groups (all: $p>0.05$). These results indicate that AFO-users have less trunk control than clinically matched Non-users and reduced trunk control is linked to falls (Honeycutt et al., 2016). While our two populations were clinically matched, AFO-users have likely more impaired ankle, which makes it unclear if the AFO is actually contributing to more falls or it is their ankle impairment. To answer this question, we evaluated AFO-users without their AFO.

AFO-users fell 6.5% more often without their AFO, however the difference was not significant ($p=0.54$). Furthermore, no differences in kinematic variables were found (all $p>0.05$) except Trunk flexion velocity at step completion which was larger with AFO compared to No-AFO ($p=0.01$). These results suggest that current AFO design does not assist the stepping response. Importantly, AFO-use decreases the incidence of falls by reducing the trips/stumbles. Rather, this study suggests that AFO-use does not assist the compensatory stepping response *after* a trip has occurred.

In conclusion, our results complement the literature showing that AFO-users are at significant fall risk even when compared to clinically matched Non-users. Further, AFO-use did not improve the response during a trip-like perturbation indicating that current AFO design may not adequately address impairment highlighting the need for better devices specifically designed to enhance the compensatory stepping response required to prevent a fall.

## F32: Sensorimotor Impairments and Cortical Reorganization in a Photothrombosis-induced Perinatal Stroke Model in Mice

Sarah Y. Zhang, Greg Silasi
*University of Ottawa, Ottawa, Canada*

### Intro & Objectives:

Perinatal stroke, which occurs around the time of birth, can lead to significant motor and cognitive deficits. Using a mouse model of perinatal stroke, we sought to investigate the relationship between sensorimotor function and forelimb representation in the sensorimotor cortex.

### Methods:

A unilateral photothrombotic stroke was induced on postnatal day 7 in the primary motor cortex (M1) of Thy1-ChR2 mice. Sensorimotor function was evaluated in adulthood with a battery of behavioural tests, including tapered beam, adhesive tape test, Schallert cylinder, and Digigait. Following behavioural testing and skilled forelimb training, a transcranial window was implanted, and baseline motor maps were created through optogenetic point stimulation of both hemispheres. Additionally, forelimb somatosensory cortex (S1) activation following forepaw stimulation was quantified with laser doppler flowmetry. Motor maps and laser doppler recordings were measured again following a single pellet reaching task to evaluate the impact of skilled motor training on cortical reorganization.

### Results:

Focal M1 stroke injury in neonatal pups resulted in differences in stroke-relevant gait parameters, decreased preference for the injured paw during cylinder exploration, and increased time to remove adhesive tape. Additionally, while overall reaching success was the same between stroke and sham groups ($0.39 \pm 0.020$ vs. $0.47 \pm 0.061\%$, $p = 0.17$), stroke animals required significantly more attempts to complete a successful reach (sham: $0.67 \pm 0.085\%$ first try success rate, stroke: $0.29 \pm 0.13\%$; $p = 0.015$). Mirroring the functional impairment, cortical motor representation of both forelimbs was diminished in the injured hemisphere (30% of sham). In contrast, the magnitude of S1 flux in response to contralateral forepaw stimulation was not impaired following stroke. Finally, preliminary results suggest that skilled motor training increases map size in the uninjured, but not injured hemisphere in stroke animals (stroke: $2.91 \pm 2.36\%$, sham: $9.70 \pm 1.79\%$; $p = 0.020$).

### Conclusions:

Motor representation and output, but not the sensory-evoked hemodynamic response, is impaired in the injured hemisphere compared to sham controls. These cortical motor changes manifest in long-term motor deficits which can be detected into adulthood, mirroring the lifelong motor impairments in individuals affected by perinatal stroke. Additionally, skilled forelimb training administered in adulthood may result in reorganization of cortical motor maps.

## F33: Proprioceptive Sensitivity, Biases and Adaptability during Post-Stroke Walking

Cristina Rossi[1,2], Kristan Leech[3], Amy Bastian[1,2]
*[1]Johns Hopkins University, Baltimore, USA. [2]Kennedy Krieger Institute, Baltimore, USA. [3]University of Southern California, Los Angeles, USA*

Stroke commonly results in motor and proprioceptive impairments which can affect gait function. In particular, asymmetric movements (e.g. unequal step lengths, stance times) are typical deficits of post-stroke gait that persist in 25-50% of individuals even after conventional therapy. Asymmetric walking is associated with instability and increased energy cost; hence, it is important that we develop targeted rehabilitation interventions that restore gait symmetry.

Emerging evidence suggests that impaired proprioception after stroke may negatively impact the ability to reduce gait asymmetry. For example, persons post-stroke must be able to perceive small changes in leg motions in order to improve their gait in response to instructive feedback commonly provided during therapy. Despite the essential role of proprioception for functional movement and stability, previous work has not thoroughly measured post-stroke proprioceptive dysfunction manifested specifically during walking. Furthermore, perceptual deficits are not fully addressed by the current rehabilitation interventions.

Here, we developed a two-alternative forced-choice task that allowed us to measure proprioception during gait. Specifically, we measured bias and sensitivity in the perception of leg velocity using a split-belt treadmill in persons post-stroke and older controls. A large bias indicates that the participant systematically feels that the velocities of their leg motions are symmetric when in reality they are not. A low sensitivity indicates that the participant is not able to perceive small changes in the velocities of leg motions. Generally, persons post-stroke showed a larger bias and lower sensitivity in their perception of leg motions compared to healthy controls. Individual participants varied in their impairments, with some exhibiting both worse bias and sensitivity than controls, and others exhibiting impairments in only one domain. Collectively, these findings revealed that persons post-stroke have marked impairment in proprioception during gait.

We then asked if adaptive learning on the split-belt treadmill could modify perceptual biases after stroke. Previous work has shown that, when healthy participants adapt on a split-belt treadmill (with one leg walking faster than the other), they recalibrate their perception of leg speed so that they inaccurately feel that one leg (the leg that walked faster in adaptation) moves slower than it actually does. To assess whether persons post-stroke also recalibrate leg speed perception, we repeated the perceptual task in the same stroke participants after they walked for 10 minutes with one treadmill belt moving twice as fast as the other. We found that all stroke participants exhibited a robust perceptual recalibration. This indicates that adaptive learning can be used to improve, at least temporarily, biases that occur in the perception of leg motion after stroke. Overall, our study proposes a new methodology to test and improve proprioception during gait in persons post-stroke.

## F34: Energy Recovery During Gait with Powered Assistance for Individuals with Cerebral Palsy: A pilot study on the impact of increased ankle power

Benjamin Conner[1], Zachary Lerner[2]
[1]*University of Arizona College of Medicine - Phoenix, Phoenix, USA.* [2]*Northern Arizona University, Flagstaff, USA*

### Introduction:

Cerebral palsy (CP) is a movement disorder characterized by impaired neuromuscular control due to injury of the developing brain. This neuromuscular disorder impacts the efficiency of movement, with the energetic cost of walking up to threefold higher compared to healthy individuals [1]. One theory for this higher cost is a lack of energy transfer throughout the gait cycle. It has been suggested that this occurs due to reduced ankle power that causes excessive ankle dorsiflexion and knee flexion, leading to a loss of kinetic energy in the stance phase, and necessitating increased muscle activity to elevate the center of mass (COM) for foot clearance [2]. To date, however, this hypothesis has not been tested. The purpose of this pilot study was to determine the effect of increased ankle power on energy recovery during gait in individuals with CP. We hypothesized that increasing ankle power to reduce metabolic cost would also lead to improved energy recovery.

### Methods:

Five individuals with CP (5 – 35 years old), Gross Motor Function Classification System levels I - III were recruited for a study to evaluate the feasibility of a powered ankle exoskeleton [3] and the data collected was used for this analysis. Level of ankle assistance was modified until a maximum decrease in metabolic cost from baseline walking was observed. An energy recovery factor (R, Eq. 3) quantified the exchange between kinetic (KE) and potential energy (PE) of the COM movement by considering the external work ($W_{ext}$, Eq. 1) on the COM and the work done by the COM ($W_{ne}$, Eq. 2) [2].

$$W_{ext} = \sum( |\Delta PE + \Delta KE | ) \quad \text{(Eq. 1)}$$

$$W_{ne} = \sum( |\Delta PE | + |\Delta KE | ) \quad \text{(Eq. 2)}$$

$$R = 100 \cdot (W_{ne} - W_{ext})/W_{ne} \quad \text{(Eq. 3)}$$

R and the metabolic cost of walking were compared between baseline and assisted conditions using a paired two-tailed *t* test with a significance level set at $\alpha < 0.05$.

### Results:

Net metabolic cost of transport during the assistive condition decreased significantly by 18.7 ± 4.8 % ($p = 0.011$) compared to baseline [3], while there was no significant difference (-8.2 ± 13.5%, $p = 0.244$) in energy recovery (R) between conditions.

### Discussion:

The findings from this study did not support our hypothesis that increasing ankle power would reduce metabolic cost by improving energy recovery. Instead, these findings suggest that a powered ankle exoskeleton can reduce metabolic cost through other mechanisms (e.g. reduced muscle activity) besides improved energy recovery. More research is needed to assess how acclimation time and gait speed may affect a user's energy recovery during assisted walking.

### References:

[1] Rose J et al. *Dev Med Child Neurol* 1990;32:333–340.

[2] Bennett BC et al. *Arch Phys Med Rehabil* 2005;86:2189–2194.

[3] Lerner ZF et al. *EEE Trans Neural Syst Rehabil Eng* 2018;26:1985–1993.

## F35: Novel, Academically-focused Cognitive Rehabilitation Program Provides a Ramp to College Success for Young Adults with Acquired Brain Injury

Natalie Gilmore, Swathi Kiran
*Boston University, Boston, USA*

*Background:*
Young adults are a frequently affected and growing population to suffer acquired brain injury (ABI).[1,2] ABI often leads to chronic impairments in cognitive-linguistic domains[3,4] essential for academic success, making college difficult for young adults after injury.[5,6] While cognitive rehabilitation (CR) is the gold standard of care,[7] limited CR services that are sufficiently intensive, salient and specific[8,9] to support college-bound young adults with ABI currently exist. Intensive Cognitive-Communication Rehabilitation (ICCR) was specifically developed to fill this gap in care. In an initial efficacy study,[10] ICCR students exhibited gains in cognitive-linguistic function, classroom performance, life participation and quality of life. However, these findings necessitate replication with a larger participant sample.

*Objective:*
To evaluate if young adults with ABI demonstrate longitudinal gains in cognitive-linguistic functioning after ICCR.

*Methods:*
Eighteen young adults (11 Male) with chronic ABI (TBI = 11; Stroke = 6; Tumor = 1) were recruited to participate in this study (Intervention group = 12; Active Control group = 6). Participants ranged in age from 21 to 35 years and months post onset from 13 to 158 months. All participants underwent a standardized assessment battery including the 1) Western Aphasia Battery-Revised[11] (WAB-R); 2) Repeatable Battery of Neuropsychological Status Update[12] (RBANS); 3) Scales of Cognitive Communicative Ability for Neurorehabilitation[13] (SCCAN); and 4) Discourse Comprehension Test[14] (DCT) before and after each intervention/no-intervention period to evaluate their cognitive-linguistic performance. The intervention group participated in ICCR six hours/day, four day/week for 12-week semester(s) including: 1) classroom-style lectures; 2) metacognitive strategy instruction/application; 3) individual therapy; and 4) technology training. The active control group continued their everyday routines, but abstained from intensive CR and/or formal academics. To assess for an intervention effect, linear mixed effects regression models were performed separately for each participant group and assessment measure. Accuracy on the assessment measure served as the dependent variable with semester as an independent predictor variable, the total *n* of timepoints contributed as a covariate, and participant as a random intercept.

*Results:*
Semester significantly predicted accuracy on all six metrics for the intervention group, indicating a cumulative benefit of ICCR. The active control group only significantly improved on three of the six metrics, suggesting that ICCR was largely responsible for gains seen in the intervention group. The covariate did not significantly predict accuracy in any of the analyses. Furthermore, a number of participants in the intervention group returned to college, but none in the active control group enrolled. *Conclusio*n. Young adults with chronic ABI demonstrated significant longitudinal gains in cognitive-linguistic function over the course of multiple semesters of a novel intensive, contextualized CR program. ICCR serves as a first step in filling the gap in CR services for college-bound young adults with ABI.

F36: Differential Effects of Internal Versus External Focus of Attention on Action Planning and Execution in Patients with Right and Left Hemispheric Stroke

Shailesh Kantak, Tessa Johnson, William Marsh
*Moss Rehabilitation Research Institute, Elkins Park, USA*

Anticipatory planning of multistep actions allows the performer to choose initial actions in the series to ensure a comfortable final position optimal for the task goal. The extent to which the side of brain damage (right vs. left) affects the planning of multistep actions after stroke is unknown. During therapy after stroke, clinicians often provide instructions and/or demonstrations to improve motor performance. An influential modulator of motor performance is the focus of attention during instruction/demonstration with mounting evidence in neurotypical adults to indicate that internal focus of attention may be detrimental to motor performance. In the present study, we investigated the comparative effects of instruction using internal versus external focus of attention on motor planning and execution of initial posture during a two-step motor task in individuals with right and left brain damage secondary to stroke. Forty one individuals (10 left brain-damaged (LBD), 11 right-brain damaged (RBD), 20 controls) performed a functional goal-directed two-sequence task, consisting of reaching and grasping a horizontally-placed dowel, turning it to vertical and placing a specified end of the dowel into a corresponding target hole. Participants with stroke performed the task with their ipsilesional hand while controls matched their hand to that used by stroke participants (10 left, 10 right). Two conditions were tested in each individual. In the external-focus condition, instructions were directed to task-relevant characteristics of the action goal, (e.g., red end of the dowel to go in red target hole). Depending on the starting position of the red end of the dowel, optimal grasping posture may be overhand (OH) or underhand (UH). In an internal-focus condition, instructions were directed to the posture of the body part needed to grasp the dowel (e.g., thumb up for an UH grasping posture). During external-focus condition, LBD group were significantly slower in planning of the initial grasp aperture (longer time to peak aperture) than the RBD group for the UH, but not the OH optimal condition (significant group X optimal posture interaction). Further, internal-focus instruction significantly impaired the planning of initial grasp relative to external-focus instruction in the LHD group but not the RHD group (significant group X instruction interaction, $p=0.003$). Importantly, deficits in planning during internal-focus instruction did not relate to comprehension; however significantly related to gesture recognition task in the apraxia battery ($r=0.97$). Subtraction map analyses suggested that the lesion in the premotor cortex and parts of caudate nucleus of the left hemisphere were associated with planning deficits in the internal-focus condition. Our findings indicate that the effects of instruction and demonstration that provide reference to a posture of the body part involved in motor planning and execution in stroke survivors may differ depending on lesion side.

## F37: Implicit and Explicit Locomotor Learning in People with Parkinson's Disease

Elizabeth Thompson[1,2], Margaret French[2], Carole Tucker[1], Darcy Reisman[2]
*[1]Temple University, Philadelphia, PA, USA. [2]University of Delaware, Newark, DE, USA*

### Background:

Parkinson's disease (PD) affects multiple body systems, leading to problems with moving as well as with learning new movement patterns. Past motor learning research in PD has focused on arm reaching, finding that people with PD are capable of both implicit learning (sensorimotor adaptation) and explicit learning (using conscious strategy or instruction) though learning may be slower or less complete than healthy adults. However, little is known about how motor learning problems may manifest in walking. As walking is often impaired in people with PD, it is necessary to understand how people with PD learn new walking tasks. The purpose of this work was to compare locomotor learning in explicit and implicit tasks in people with PD versus healthy adults.

### Methods:

Ten volunteers with PD (mean age 65.4 ± 6.54 years, 7M/3F, all Hoehn & Yahr stage 2) and two age matched healthy volunteers (ages 59 and 57, 1M/1F) have participated thus far. Volunteers completed two sessions of treadmill walking with motion capture measuring step length. One session consisted of an implicit adaption task using a split-belt treadmill paradigm, while the other session was an explicit learning task using verbal instructions and visual feedback regarding step length. Split-belt walking required participants to adjust to a perturbation and return to step length symmetry, while the visual feedback required participants to take a longer step with one leg to match targets on the screen. Order of testing sessions was counterbalanced by participant, and number of training steps per participant was the same across both paradigms.

### Results:

In split-belt adaptation, all participants showed asymmetrical stepping when the belts were first split. Over the course of training, both groups became more symmetrical. Healthy adults improved their step symmetry index (SSI) from -0.040±0.049 to 0.028±0.019, while the group with PD only improved their SSI from -0.146±0.115 to -0.056±0.076 (where an SSI of 0.00 represents symmetry). In the visual feedback task, the healthy adults increased their step length after training from 60.6±0.049 cm at baseline to 67.9±0.070 cm after training, resulting in healthy participants hitting the target. The group with PD was also able to increase their step length but did not change not sufficiently to hit the target (mean change from 47.1±12.5 cm at baseline to 52.4±12.7 cm after training).

### Conclusions:

Individuals with PD were able to learn a new walking pattern through both implicit sensorimotor adaptation and more explicit learning using visual feedback, though total amount of learning was reduced compared to neurologically intact, age matched participants. Understanding how walking tasks are best learned in those with PD versus those without can inform the development of rehabilitation interventions to help people with PD improve their walking.

## F38: Developing an Automated System for Identifying Upper Extremity Rehabilitation Exercise Type and Quantifying Exercise Dose Using Biometric Sensors and Machine Learning

Noah Balestra[1], Kyle Choi[2], Tanzeem Choudhury[3], Ania Busza[4]
*[1]University of Rochester, Rochester, NY, USA. [2]Cornell University, Ithaca, NY, USA. [3]Information Science Department, Cornell University, Ithaca, NY, USA. [4]Department of Neurology, University of Rochester, Rochester, NY, USA*

### Objective:

To develop an automated system that identifies specific upper extremity exercises and tracks the number of exercise repetitions in post-stroke patients with moderate arm weakness in order to measure patient rehabilitation exercise "dose".

### Background:

While stroke rehabilitation research and treatment generally involve measuring the dosage of stroke rehabilitation using "time spent in therapy", studies that measure the actual amount of exercise performed during rehabilitation show that the same amount of time can represent a wide range of patient participation and numbers of repetitions. Advanced biometric technology, in this case the MC10 BioStampRC® sensors, may provide ways to directly measure the number of patient completed exercises, or exercise "dose". These sensors can record accelerometer, electromyography, and gyroscope data to monitor patient activity.

### Design:

29 total subjects have been enrolled in the study to date (Mean age: 61 years old), 21 of which were post-stroke patients with moderate arm weakness (all during the acute/subacute stroke period with MRC strength scale score: 3-4). The remaining 8 subjects were healthy controls with no arm weakness. Three MC10 BioStampRC® wearable sensors were placed on subject's arms to record a combination of either triaxial accelerometry and electromyography or triaxial accelerometry and gyroscope data during three prompted upper-extremity exercises and resting periods. Using the accelerometer and gyroscope data and machine learning, an algorithm was trained to differentiate between three different movements and provide a count of the number of repetitions performed for each exercise.

### Preliminary Results:

The model was able to discriminate between three pre-selected exercises effectively when used on preliminary data, including healthy controls and patients with moderate arm weakness. Overall classification accuracy ranged from approximately 95% - 99.5% depending on which subject's data was analyzed. In terms of the model's ability to count the repetitions, comparison of the manual counts versus model counts of five healthy subjects' repetitions showed that the program was able to count effectively, with "leave-one-subject-out cross-validation" (LOOCV) accuracy ranging from 94.24% to 98.35%.

### Conclusion/Future Direction:

While the preliminary results are promising, the current classification algorithm has a relatively high rate of false negative identification. We are currently evaluating if this can be ameliorated by incorporating electromyography data into the algorithm. Ultimately, we hope to develop an automated system to more accurately measure exercise dosage in stroke rehabilitation (rather than simple tracking of time spent in therapy). Such a system can then be used in future studies to study and account for the effect of rehabilitation exercise dosage on post-stroke motor recovery.

## F39: Optimizing Video Game Design for Stroke Rehabilitation: A systematic review of important game parameters

Nathan Pinnette[1], Ania Busza[2]
*[1]University of Rochester, Rochester, USA. [2]Department of Neurology University of Rochester, Rochester, USA*

Introduction:
Stroke is one of the leading causes of disability for adults in the United States. Previous research suggests that patients may have improved post-stroke motor recovery if they engage in highly repetitive exercises of their affected limbs. In recent years there has been increased interest in using video games in rehabilitation to encourage patients to perform exercises more often and for longer periods of time, however research examining optimal video game design for patients who have suffered a stroke is relatively limited. We review prior studies that examine how specific video game parameters affect stroke patient motivation and game usage, and identify areas for future research.

Objectives:
We conducted a systematic review of selected articles to identify the important design parameters of video games in motivating stroke patients to play and perform their exercises more frequently and for longer periods of time.

Methods:
PubMed and Google Scholar were utilized to perform a systematic literature review on the topic of designing video games to be motivational for stroke patients. A preset guide was used to determine the usability of each article.

Results:
From the databases we found over 23,200 titles. Utilizing the preset guide 44 articles were identified and 12 were included in the systematic review. These articles included 5 surveys/questionnaires, 1 video game group intervention, 3 had therapy session based studies, 1 workshop, and 4 had patients play video games and analyzed the patients as they played. These studies suggest that the important aspects of video game design for stroke rehabilitation are challenge, goals, scoring, feedback, controller, social interaction, audio/visual effects, adaptable to patient's motor skills, calibration for range of motion, varying difficulty, and response time. Conclusions: There are many important design parameters that motivate stroke patients to play video games more frequently and for longer periods of time. When designing a video game for stroke rehabilitation it is important to look at each video game aspect and make sure that it accounts for varying skill levels, poor vision, poor motor skills, poor response time, and it is important to make sure that the game and controller are friendly. Future studies are needed to clarify how these parameters are affected by patient-specific factors, such as age, prior history of gaming, and time since stroke onset.

## F40: Decreased Excitability of Contralesional Cortex in Individuals with Moderate to Severe Upper Limb Impairment

Mary Ellen Stoykov[1,2], Fabian David[4], Erin King[5], Daniel M. Corcos[4], Sangeetha Madhavan[6]
*[1]Northwestern University, Dept. of Physical Medicine and Rehabilitation, Chicago, USA. [2]Shirley Ryan AbilityLab, Arms & Hands Lab, Chicago, USA. [4]Northwestern University, Department of Physical Therapy and Human Movement Science, Chicago, USA. [5]Northwestern University, Chicago, USA. [6]University of Illinois at Chicago, Department of Physical Therapy, Chicago, USA*

### Background:

The role of the contralesional cortex in post-stroke upper limb recovery is not well understood. McCambridge et al, 2018[1] suggest that the role may vary depending on magnitude of impairment and that more severely impaired stroke survivors rely on the contralesional cortex for control of the more affected upper limb. The present study examines baseline data from an intervention study (Clinical trial # NCT03517657) for individuals with moderate to severe upper limb hemiparesis (FMUE score between 23-38). Obtaining resting motor thresholds (RMTs) from the ipsilesonal hemisphere is extremely difficult and often not possible in this cohort of stroke survivors. Therefore, RMTs of the contralesional cortex were obtained. Motor evoked potential status (MEP+ or MEP-) was determined by the presence of active MEPs recorded during bilateral isometric wrist extension. Baseline RMTs from contralesional cortex were higher than expected. We examined possible relationships between behavioral measures, cortical excitability measures, and demographic characteristics.

### Objective:

The authors sought to identify mechanisms related to the observed high resting motor thresholds (RMT) in the contralesional hemisphere of participants with moderate to severe upper limb impairment.

### Methods:

Our dependent outcome was RMT of the contralesional hemisphere expressed as a percentage of maximal stimulator output. Our independent outcomes included both categorical and continuous measures. The former included included MEP status (positive or negative) of the ipsilesional hemisphere as defined by Stinear et al, 2017[2]; persistence of ipsilateral silent period (ISP) from ipsilesional on to the contralesional hemisphere; sex; and side of lesion. Continuous measures included depth of the ISP, duration of ISP, age, and FMUE Test of Function score for the affected upper extremity. We used stepwise linear regression to analyze the data.

### Results:

The only variable that was retained in the model was MEP status. All other variables did not meet the criteria to stay in the model. MEP status was the only significant predictor of contralesional resting motor threshold ($F_{1,21} = 9.173$, $p = 0.006$). On average, the RMT was 17% (95% CI: 6% to 30%) greater in the MEP negative group when compared to the MEP positive group. The adjusted R squared was .271, indicating that 27% of the variance in RMT of contralesional cortex is explained by MEP status from ipsilesional hemisphere. No other measure (behavioral, cortical excitability, or demographic) predicted contralesional RMT.

### Conclusion:

We found that, in this cohort of individuals with moderate to severe post-stroke upper limb impairment, RMTs of the contralesional cortex were significantly higher in individuals with ipsilesional MEP negative status. The findings of this study do not support the inter-hemispheric competition model. They are consistent, however, with more recent evidence that stroke may have more systemic effects on the brain and its networks.[3]

## F41: Flexion Synergy is the Principal Detriment to Reaching Function in Individuals with Chronic Moderate to Severe Stroke

Grace C. Bellinger, Michael D. Ellis
*Northwestern University, Chicago, IL, USA*

Chronic stroke survivors demonstrate a myriad of impairments impacting reaching function including flexion synergy, passive range of motion limitations, spasticity (i.e., hyperactive stretch reflexes), and weakness. Flexion synergy results in loss of independent joint control due to the abnormal coupling of shoulder abductors with elbow, wrist, and finger flexors. The relative and concurrent contributions of each of the underlying factors has not yet been quantitatively explored in depth. 34 individuals (23 males, 58.3 ± 10.8 years old) with chronic stroke (11.8 ± 8.3 years post-stroke) participated in the study. The upper extremity Fugl-Meyer Motor Assessment scores (26 ± 7) ranged from 49 to 15 indicating moderate to severe generalized levels of impairment, respectively. Reaching function was measured with a robotic admittance-controlled end-effector device and defined as maximum reaching distance against gravity. A multiple linear regression model was implemented to investigate the constitutive impairments limiting reaching function. The regressors were quantified using kinematics, kinetics, and electromyography (EMG). The regressors included: 1) maximal shoulder abduction and elbow extension strength [normalized to the unaffected side], 2) spasticity-related biceps activation [measured as the increase in EMG occurring after elbow extension onset during reaching at a standardized load], 3) flexion synergy [measured as the highest shoulder abduction load at which the participant could successfully lift the arm and reach two standardized targets], and 4) passive range of motion at the elbow. A significant regression equation was found ($F(6,18) = 3.724$, $p = 0.014$) with an $R^2$ of 0.554. Reaching function (Mean ± SD; 0.608 ± 0.358) was significantly correlated with flexion synergy emergence threshold (0.310 ± 0.244, $r = 0.634$, $p = 0.001$), shoulder abduction strength (0.557 ± 0.193, $r = 0.390$, $p = 0.023$), and elbow extension strength (0.437 ± 0.186, $r = 0.407$, $p = 0.017$). Passive range of motion, active flexor spasticity, and flexion synergy takeover threshold did not significantly correlate with reaching function. A subsequent model dropping non-correlated regressors found a significant regression equation ($F(3,22) = 6.858$, $p = 0.002$) with an $R^2$ of 0.483. Flexion synergy emergence threshold was the only significant regressor in both the complete (standardized beta = 0.594, $p = 0.007$) and reduced (standardized beta = 0.521, $p = 0.005$) models. The results indicate that impairments such as weakness, flexor spasticity, and passive range of motion limitations may not contribute to reaching dysfunction to the same extent as flexion synergy. The significant standardized beta coefficient can be interpreted as a one unit increase in the flexion synergy emergence threshold (i.e., less synergy impairment) being associated with a 0.521 unit increase in reaching function. The findings of this study suggest that prioritizing flexion synergy impairment is likely to have the greatest impact when attempting to restore reaching function in chronic moderate to severe stroke.

## F42: The Relation Between Function Connectivity and Clinical Outcomes in Adult Stroke Survivors Undergoing Exoskeleton Upper Limb Home Therapy

Melissa Sandison[1,2], Peter Lum[1,2]
[1]*The Catholic University of America, Washington DC, USA.* [2]*RERC-DC, Washington DC, USA*

### Background:

Optimization of stroke rehabilitation techniques and prescription is dependent on improving our knowledge of brain plasticity. Few studies have investigated plasticity via EEG associated with motor outcomes of robotic therapy. This study aims to investigate brain plasticity, via functional connectivity (COH), of stroke patients undergoing at home robotic upper-limb therapy. Additionally, we aim to understand stroke-specific changes of COH utilizing EEG, and identify biomarkers which predict a patient's clinically-measurable response to the robotic intervention.

### Methods:

Six hemiparetic chronic stroke patients (mean age= 55, 3males, post stroke=3.8 years) underwent an 8 week upper-limb rehabilitation program using a wearable, high degree of freedom, spring powered hand exoskeleton, HandSOME-II [1]. The Fugl Myer (FM) test was completed pre and post therapy to assess changes in upper-limb impairment. Additionally, pre and post therapy intervention, EEG signals were recorded continuously from a 28 Ag/AgCl electrode cap. Signals were recorded during three minutes of wakeful rest and during the Nine Hole Peg Test. Primary outcome measures were resting-state COH (COHrest) and task-related COH (TRCoh). Linear regression analyses were undertaken to identify plasticity and biomarkers that predicted response to robotic therapy.

### Results:

The results showed plasticity elicited from HandSOME-II therapy was correlated with changes in motor function. Specifically, increases in interhemispheric frontal-central alpha COHrest, and contralesional frontal-central alpha COHrest correlated with improved motor function ($p<0.05$, $r^2 = 0.69$ and 0.66, respectively). We also identified baseline biomarkers; higher baseline contralesional frontal-central beta COHrest and lower baseline contralesional frontal-parietal alpha COHrest were associated with greater gains in motor function ($p<0.05$, $r^2 = 0.81$ and 0.67, respectively). Initial level of impairment or time since onset of stroke did not correlate with response to therapy or plasticity. We found no significant interaction between TRCoh and motor improvements. Improvement in FM varied for each patient, ranging from 0-10 point increase in upper-limb score.

### Conclusions:

The range of changes in FM score highlight the heterogeneous nature of stroke recovery, emphasizing the need for a measure that can predict the capacity for rehabilitation and evaluation. Resting state alpha and beta COH are potential biomarkers for predicting motor outcome and quantifying brain reorganization, while initial impairment and time since stroke did not predict recovery in our sample. The ability to assess the neuronal network at rest has vast implications in stroke rehabilitation and research focusing on plasticity, particularly in severely impaired stoke survivors where completing a motor task may not be possible. Increased contralesional FC associated with improved motor outcome found in this study could indicate a supportive compensation strategy of the damaged hemisphere[2]. We showed that home based exoskeleton therapy using the HandSOME-II device elicits plasticity associated with motor function improvements, validating its use.

## F43: Excessive Neural Activation in Cerebellar Network during a Non-Symptomatic Task in Adductor Spasmodic Dysphonia: An fMRI and TMS Study

Yi-Ling Kuo[1], Mo Chen[2,3], Rebekah Summers[2], Cecília Prudente[2], George Goding[4], Sharyl Samargia[5], Christy Ludlow[6], Teresa Kimberley[1,7]

*[1]Brain Recovery Laboratory, Massachusetts General Hospital Institute of Health Professions, Boston, USA. [2]Divisions of Physical Therapy and Rehabilitation Science, University of Minnesota, Minneapolis, USA. [3]Non-invasive Neuromodulation Laboratory, MnDRIVE Initiative, University of Minnesota. [4]Department of Otolaryngology-Head and Neck Surgery, University of Minnesota, Minneapolis, USA. [5]Department of Communication Sciences and Disorders, University of Wisconsin River Falls, River Falls, USA. [6]Department of Communication Sciences and Disorders, James Madison University, Harrisonburg, USA. [7]Department of Physical Therapy, Massachusetts General Hospital Institute of Health Professions, Boston, USA*

### Introduction:

Adductor spasmodic dysphonia (AdSD) is a focal task-specific laryngeal dystonia characterized by spasms in the thyroarytenoid (TA) muscles, leading to vocal fold hyperadduction. People with AdSD have difficulty controlling voluntary sound production in the vocal folds, which leads to difficulty speaking. Reduced inhibition in the primary motor cortex (M1) could contribute to involuntary movements in focal dystonias, including AdSD. Recent work has shown that decreased intracortical inhibition in the laryngeal motor cortex (LMC), measured by transcranial magnetic stimulation (TMS), is associated with increased blood-oxygen-level dependent (BOLD) activation, measured by functional magnet resonance imaging (fMRI), in the LMC over the left hemisphere during phonation (i.e. symptomatic task) in people with AdSD. Other work has demonstrated reduced intracortical inhibition in the M1 representing asymptomatic body parts. However, it is unclear if the widespread reduced intracortical inhibition in asymptomatic muscles is associated with BOLD activation during task fMRI in a whole brain analysis in people with AdSD. Thus, the purpose was to compare the BOLD activation during finger-tapping (i.e. asymptomatic task) between people with AdSD and age-matched controls.

### Methods:

16 people with AdSD (63.9 ± 4.8 yrs; 10 females; all right-handed) and 16 controls (51.5 ± 7.9 yrs; 5 females; all right-handed) participated this study over two visits. On Day 1, participants performed an fMRI finger-tapping task at a constant and comfortable speed that alternated between left and right index finger movement and rest. On Day 2, TMS-evoked cortical silent period (cSP) and short-interval intracortical inhibition (SICI) were measured in the left M1 for the first dorsal interosseous (FDI). BOLD activation was compared between the two groups using a fixed effect general linear model (GLM) to determine the group (AdSD vs controls) by activation interaction. Voxel-wise ($Z > 2.5$ for between group analysis) significance was set to $p < 0.01$ (multiple comparison corrected). Intracortical inhibition measures (cSP and SICI) were compared between AdSD and controls using independent *t* tests.

### Results:

People with AdSD demonstrated significantly decreased hand cSP compared to controls (88.4 ± 22.6 ms vs 111.2 ± 31.3 ms, $p = 0.025$). Greater BOLD activation during finger tapping was observed in bilateral cerebellum (primarily anterior lobe), right motor cortex and left somatosensory cortex in people with AdSD compared to controls. There were no regions of greater activation in controls vs AdSD.

### Conclusion:

Widespread over activation in the cerebellum, motor cortex and somatosensory cortex during an asymptomatic task is complementary evidence to TMS-measures of reduced inhibition in cortical excitability in people with AdSD. The highly activated cerebellum, which is primarily a hub of inhibitory processing, may contribute to the lack of suppression of involuntary movement in focal dystonia.

F44: Characterization, Identification, and Mitigation of Movement Artifacts in Electroencephalographic Measurements Toward Robot-aided Neuromuscular Assessment

Sebastian Rueda-Parra, Eric T. Wolbrecht, Joel C. Perry
*University of Idaho, Moscow, USA*

Electroencephalography (EEG) has become one of the most widely used tools for understanding the brain at structural, functional, behavioral, physiological, and pathological levels. However, reliable data acquisition is still a problem that emerges during recording sessions [1]. EEG data is highly susceptible to artifacts introduced by unwanted movements of the user, the EEG setup, unwanted bioelectric potentials, or from external sources of electromagnetic noise, all of which have considerable impact on data integrity, making further decomposition and analysis of signals challenging to achieve. For decades, the state of the art in artifact identification and removal has relied on visual inspection of cerebral signals in the time domain. Only recently have researchers begun exploring alternate methods to better automate the identification process with common artifacts [1,2]. In this study, we aim to characterize a wider array of frequently observed artifacts present during task-related EEG and EMG (electromyography) recordings with a focus on the motor cortices toward reliable use of EEG measures in functional assessment of the arm and hand. Outcomes from the study will contribute to the BLUE SABINO project [3], where our objective is to assess motor function in individuals with neurological damage.

To record common artifacts, sets of emulated artifacts were repeated, including: involuntary contractions, movements (physiological artifacts), undesired motions of the recording hardware, and changes in the environment of the recording (extra-physiologic artifacts). The EEG montage for data acquisition consists of a bio-signal recording system from g.tec (Graz, Austria) for signal acquisition and amplification in both EEG and EMG bio-signals. In this particular case, an array of 36 EEG electrodes were used with higher density along the motor and premotor cortices, 2 bipolar EOG channels monitored vertical and horizontal eye movements, and 4 bipolar EMG channels monitored activation of select muscle groups in the arm.

Recorded signals were pre-processed before feature extraction in order to obtain clean and reliable data that permitted artifact analysis. Utilizing several domains of signal decomposition allowed a better characterization of time, frequency, time-frequency, spatial, and independent component analysis (ICA) features. Feature characterization provides meaningful insight on a variety of aspects, such as the impact that each individual artifact has on recorded data, the sensitivity of specific electrode locations to a given stimuli, patterns of EMG activation that may be abnormal for a given task, reactive frequency bands of activity that do not belong to the experiments, and ERPs that represent noisy data. Improved characterization methods will lead to implementation of algorithms that automatically target trials with artifacts. The resulting knowledge will be applied in future experiments to improve electrode montage selection as well as design tasks and protocols for data acquisition and processing that are less prone to be affected by artifacts.

F45: Finger Force Perception during Pressing Tasks: Comparison of force matching, hypothetical control variables matching, and psychophysical reports

Cristian Cuadra[1,2], Mark Latash[1]
*[1]Penn State, State College, USA. [2]Universidad Andres Bello, VINA DEL MAR, Chile*

We used the hypothesis that neural control of movement can be described as specifying time patterns of spatial referent coordinates (RC) for the effector, while abundant afferent signals report on deviations of the effector from RC.

In the first experiment we explored a recently introduced scheme of perception based on the concept of iso-perceptual manifold (IPM) in the combined afferent–efferent space of neural signals. Within this scheme, we assume that afferent signals from multiple sources are estimated within a frame of reference provided by the multiple ongoing efferent processes that can be adequately described as time-varying spatial reference coordinates. An IPM is equivalent to stable perception of a physical variable. We used force-matching tasks between the two hands, and verbal reports, to explore finger force perception in a two-finger pressing task. The main hypothesis was that accuracy would be lower and variability higher during individual finger force matching in a two-finger task compared to one-finger tasks. The subjects produced accurate force levels under visual feedback by pressing with either two fingers or one of the fingers of a hand (task-hand). They tried to match the total two-finger force or individual finger forces by pressing with the other hand (match-hand, no visual feedback). Also, we used verbal report within a psychophysical scale on the level of force that the task-hand was producing. The match-hand overestimated the force of the task-hand at low forces and underestimated it at high force. The verbal report consistently overestimated the task-hand force, with larger errors for higher forces. These findings confirm our main hypothesis by showing that perception of individual finger forces can vary in multi-finger tasks within a space (IPM) corresponding to veridical perception of total force.

In the second experiment we explored the changes in hypothetical control variables. We tested hypotheses related to the perception of control variables translated: apparent stiffness (K) and referent coordinate (RC). The “inverse piano” device was used to estimate control variables. We used force-matching tasks between the two hands to explore finger force perception in a two-finger pressing task. Subjects were asked either to double the force or co-contract the forearm muscle of the task hand, after visual feedback of its force was removed. Then, the subjects were asked to match the force with other hand. Force doubling was accompanied by RC increase, co-contraction was not. RC was much higher in the match hand. K did not change during force doubling but increased in co-contraction. Furthermore, K was smaller in the match hand compared to the task hand, particularly for co-contraction trials. The results also support the scheme of control with two classes of neural variables, RC and K.

F46: The Neural Mechanisms Underlying tDCS Effects in PPA: Evidence from resting-state functional network analysis
***Presidential Award Finalist***

Yuan Tao[1], Brenda Rapp[2], Kyrana Tsapkini[3]
*[1]Johns Hopkins University, Baltimore, USA. [2]Department of Cognitive Science, Johns Hopkins University, Baltimore, USA. [3]Department of Neurology, Johns Hopkins School of Medicine, Baltimore, USA.*

Anodal transcranial direct current stimulation (tDCS) over the left inferior frontal gyrus (LIFG) has been shown to have augmentative benefits in aphasia rehabilitation (Fridriksson et al., 2018). We and others have recently shown that this is also the case in progressive disorders such as primary progressive aphasia (PPA) (Roncero et al., 2017; Tsapkini et al., 2018). However, the underlying neural mechanism is not understood. Recently, in a double-blind, sham-controlled trial (NCT02606422), we found that the tDCS-based behavioral benefits were modulated by decreased resting-state functional connectivity (RSFC) between the stimulation site (LIFG) and temporal and parietal regions, suggesting tDCS may serve to strengthen functional segregation (Ficek et al., 2018).

In the present study we extend this finding by examining the whole-brain RSFC network properties with graph-theoretic methods. Specifically, we examined the *between-network connectivity* of the target brain regions using *participation coefficient* (PC), a measure which indexes the extent to which a brain region interacts with multiple functional brain networks (Guimera and Amaral, 2005).

Thirty-two PPA participants underwent language training (oral and written naming/spelling) in a crossover design. Here we present only the results of the first period, during which half (N=16) received anodal tDCS at the LIFG and half received sham, both coupled with language therapy. Resting-state fMRI data were collected before and after treatment. MRI data were also obtained from a cohort of age-matched healthy controls (HC, N=17). First, for each participant, whole-brain, pairwise FC was computed for 78 brain regions. Using the HC data, all the regions were grouped into 7 functional networks, based on which the pre- and post-treatment *participation coefficient* (PC) values of the LIFG was computed. PC changes for tDCS and sham conditions were compared with one-sample and independent t-tests. Finally, the PC changes were correlated with behavioral improvement for each group.

All tDCS and sham participants showed behavioral improvement but it was marginally larger in tDCS vs. sham (p=0.08). Regarding the PC changes of the LIFG, the tDCS group showed a significant decrease (t(15)=-2.3, p=0.04) in the connectivity of this area with the 7 functional networks, whereas the sham group showed numerical increase (t(15)=1.21, p=0.24), and a significant interaction was found between time-point and treatment group (p=0.03). Moreover, the PC increase of the sham group was positively correlated with behavioral improvement (r=0.36, p=0.09), whereas for the tDCS group there was a negative correlation (r=-0.17, p=0.28, interaction p=0.08). The opposite relationship between changes in connectivity and treatment outcome suggested that tDCS introduced qualitatively distinct neural changes that were more beneficial than those experienced by the sham group.

## F47: Theta Power is a Longitudinal EEG Spatial and Spectral Biomarker of Spontaneous Motor Recovery after Stroke

Lauren Ostrowski[1,2], A. Nicole Dusang[3,4,1], Alison Cloutier[2], Fabio Giatsidis[2], Sydney Cash[5,6], Leigh Hochberg[1,3,2,6,4], David Lin[2,1]

*[1]VA RR&D Ctr. for Neurorestoration and Neurotechnology, Dept. of VA Med. Ctr., Providence, USA. [2]Ctr. for Neurotechnology and Neurorecovery, Dept. of Neurol., Massachusetts Gen. Hosp., Boston, USA. [3]Sch. of Engin., Brown Univ., Providence, USA. [4]Carney Inst. for Brain Sci., Brown Univ., Providence, USA. [5]Dept. of Neurol., Massachusetts Gen. Hosp., Boston, USA. [6]Harvard Med. Sch., Boston, USA*

### Introduction:
Current neurorestorative therapy options to enhance upper extremity motor recovery after stroke are limited. Neurological biomarkers that reflect underlying biological processes and correlate with motor recovery could provide important surrogate clinical endpoints for stroke recovery trials. Slow-wave oscillations on EEG have been linked to cerebral dysfunction after stroke, but robust EEG biomarkers that track with upper extremity motor recovery have yet to be defined. Here, our aim is to define spatial and spectral properties of EEG that provide optimal biomarkers for upper extremity motor recovery in the first three months after stroke.

### Methods:
We recorded natural-state, high-density 128-channel EEG data in 15 patients within one week and subsequently at six weeks and three months after ischemic stroke. We used a customized semi-automated pipeline for offline EEG data pre-processing (eye-blink and artifact rejection). Spectral power was calculated in leads overlying the contra- and ipsilesional motor cortex, contra- and ipsilesional hemispheres, and over the whole scalp, in predefined bands: delta (1-4 Hz), theta (5-7 Hz), alpha (8-12 Hz) and beta (13-30 Hz). We used the Upper Extremity Fugl-Meyer Assessment (UE-FMA) to quantify upper limb motor impairment at each time point.

### Results:
Absolute theta power was the only spectral feature which correlated with UE-FMA at all timepoints (at enrollment $R^2 = 0.23$, $p = 0.067$; at six weeks $R^2 = 0.35$, $p = 0.026$; at three months $R^2 = 0.25$, $p = 0.067$, Pearson's r). The largest number of spectral correlates were found at six weeks, where relative theta power in the lesioned hemisphere had the strongest relationship of all spectral bands in all spatial regions ($R^2 = 0.63$, $p < 0.001$). Favorable change in UE-FMA linearly correlated with decrease in absolute theta power in the lesioned hemisphere between six weeks and three months ($R^2 = 0.34$, $p = 0.028$), but not between enrollment and six weeks. Finally, theta power in the lesioned hemisphere at six weeks, but not at enrollment, was predictive of UE-FMA outcome at three months (absolute power $R^2 = 0.25$, $p = 0.066$; relative power $R^2 = 0.54$, $p = 0.003$).

### Conclusion:
EEG spatial and spectral features contain useful information indicative of spontaneous upper extremity motor recovery. Theta power in the lesioned hemisphere may be an optimal cross-sectional and longitudinal spectral biomarker and may be particularly informative for motor recovery at six weeks post-stroke as opposed to the immediately acute setting.

F48: Role of Erk Phosphorylation and Retrograde Transport in Signaling Axotomy after Spinal Cord Injury

Li-Qing Jin[1], Kristen Hall[1], Samantha Lam[1], Jianli Hu[1], Michael Selzer[1,2]
[1]*Shriners Hospitals Pediatric Research Center, Lewis Katz School of Medicine at Temple University, Philadelphia, USA.*
[2]*Dept. of Neurology, Philadelphia, USA*

Activation of extracellular signal-regulated protein kinase (Erk), a member of the mitogen-activated protein kinase family, has been shown to mediate neurite outgrowth-promoting effects of many neurotrophic factors. Recently Erk has been recognized as one element of retrograde signaling complex that is transported to the cell body to illicit cell responses to stress stimuli. Most research on Erk have been conducted *in vitro* or in peripheral nerve, but are difficult to perform in mammalian CNS. To confirm the role of Erk in retrograde signaling of axon injury in the CNS, we used immunoblotting and immunohistochemistry to study the changes in phosphorylated Erk (phospho-Erk1/2) in the spinal cord, and in phosphorylated c-Jun (p-c-Jun) in the brain after spinal cord transection in the lamprey. The role of dynein and vimentin in the retrograde complex was tested by colocalization studies. Result showed: 1) phospho-Erk1/2 and p-c-Jun levels were increased 0.5 hr after spinal cord transection. A plateau (6-fold) increase was reached for phospho-Erk1/2 levels in the spinal cord at 6 hrs, whereas the p-c-Jun plateau (3-fold) in the brain was reached at 1-3 hrs. 2) Immunostaining for phospho-Erk1/2 was weak in control spinal cord. Spinal cord transection triggered an increase in phospho-Erk1/2 staining both inside axons and in the local cells in both transverse and coronal sections. The heaviest staining occurred in the 1-2 mm closest to the injury between 3-hrs and 6-hrs post-transection. 2) At high magnification, heavily stained 3-5 µm granules were seen along the courses of the large reticulospinal axons at 3 and 6-hrs post TX, most heavily concentrated in the region of the transection, becoming weaker rostrally. 3) We confirmed that axons of normal spinal cord contained little or no mRNA by oligo-dT i*n situ* hybridization for poly-A-RNA. By 3 hours post-transection increased poly(A)+RNA staining was seen inside axons near the cell body (1-2 mm), but not in distal axon (10 mm from the cell body). 4) The molecular motor dynein was colocalized with phospho-Erk1/2 in granules within the axons after spinal cord transection, but vimentin was not, even though its levels were elevated. These findings suggest that as in peripheral nerve, Erk1/2 is an important retrograde signal of axon injury in the CNS, but unlike what has been reported in PNS, vimentin may not be part of the injury signaling complex in CNS.

## F49: Amantadine Enhances Adaptive Potential in Early Adulthood Following Severe Crush Injury in Infancy

Joseph Malone, Claire Flaherty
*Penn State Health Neurology, Hershey, USA*

### Objective:
To pharmacologically manage akinetic mutism in the chronic course of recovery from severe traumatic brain injury in infancy.

### Background:
Crush head injuries involve the application of a static force over a time period of 200ms. The annual prevalence of traumatic brain injuries has been estimated to occur at 470,000 children under age of 14. In the United States, annually, over 2000 children younger than age 5 are injured in low speed vehicle run-over accidents. Of those, 100 die. Survivors potentially suffer skull fractures; subarachnoid, epidural and subdural hemorrhage; and brain contusions and lacerations[1.] Total population based health care costs for severe TBI in children are $206 million in the first 12 months.[2] Severe crush injury in infancy is associated with a neurodevelopmental sequelae of disabilities encompassing cognition, affect and personality, with behavioral changes potentially resulting in institutionalization in adulthood. Effective approaches to optimize functional independence are vital to ease the long term financial burden to society and enhance the quality of life of affected individuals.

### Study/Design:
BD was a 22 year old left-handed gentleman who survived a roll over crush injury sustained at 11 months of age. He presented for gradual regression into akinetic mutism following discontinuation of education in a learning support environment. Neuroimaging indicated severe left temporal, bilateral frontal, parietal, occipital, and cerebellar cortical encephalomalacia. Neurological exam revealed mild right sided weakness, cortical visual impairment, and RHH; sensory exam was otherwise unrevealing. There was no evidence of cortical aphasia: speech was mildly aprosodic while fluent, with intact auditory comprehension, naming and repetition. Neuropsychological assessment indicated intact verbal memory, with literacy and social cognition skills at the 6-10 year old level. Emotional health was attested to by his affection toward family and friends, as well as pets. By contrast, initiation/responsiveness was poor, with BD looking to his parents to respond for him, a progression of chronic apathy into abulia. Amantadine was titrated to 100 mg bid.

### Results:
Initiation/responsiveness increased beyond his pre-regression baseline, resulting in sustained gainful employment as a dishwasher in a local nursing home.

### Conclusions:
The psychotropic effect of amantadine is related to its antagonism of the N-methyl-D-aspartate (NMDA) receptor. It decreases the toxic effects of the glutamatergic neurotransmitter system, with evidence based pediatric benefits in attention deficit hyperactivity disorder and adult benefits for mood disorders following TBI[3]. Amantadine is well tolerated in children and adolescents, with a profile of acceptable side effects and safety for long term use. Our results indicate a need for clinical trials to explore its potential to enhance initiation/responsiveness, motivation and drive following pediatric severe TBI, executive functions crucial to functional independence in adulthood.

F50: Perturbation Training Rehabilitation of Dynamic Balance for Persons with Acquired Brain Injury: Exploratory, interventional and a neuroimaging trial

Katherin Joubran, Simona Bar-Haim, Lior Shmuelof
*Ben-Gurion University of the Negev, Beer Sheva, Israel.*

Acquired brain injury is a major cause of functional disability and is characterized by a deterioration of dynamic balance. Unpredictable ground conditions training is a novel paradigm for task-specific and challenging dynamic balance training. In this study, we investigate the effect of long-term unexpected constant balance perturbation training on dynamic balance for persons with acquired brain injury at the chronic stage, and on the associated neural networks.

We present evidence of dynamic balance improvement following 3 months of perturbation training. Then, using resting state fMRI analysis, we report that dynamic balance impairments are associated with reduced brain modularity, and that recovery is associated with increased modularity. Finally, using structural MRI analysis, we report that persons with ABI show a reduction in the volume, area and thickness of cortical and subcortical regions when compared to healthy age-matched subjects, suggesting that motor impairments in ABI could be associated with increased atrophy following the brain damage. Overall, perturbations training can improve dynamic balance at the chronic stage. Our results indicate that both the impairment and the recovery of dynamic balance in ABI are associated with brain regions that are distant to the area of the initial brain injury.

## F51: Intense Therapy after a Left Hemisphere Stroke Leads to Structural Adaptation in Right-hemisphere

**Fletcher H. McDowell Award Finalist*

Sebastien Paquette, Andrea Norton, Gottfried Schlaug
*Beth Israel Deaconess Medical Center / Harvard Medical School, Boston, USA*

Although the specific neural mechanisms underlying post-stroke recovery of speech-motor function have yet to be empirically defined, two prominent hypotheses inform our current understanding (Schlaug, 2018): (1) the perilesional hypothesis suggesting recruitment of healthy perilesional cortex forms a new network of regions in the affected hemisphere (e.g., Belin, et al., 1996; McKinnon et al., 2017), and (2) the "right-shift" hypothesis proposing engagement of homotopic regions in the undamaged right hemisphere facilitate recovery of speech-motor function (e.g., Heiss and Thiel 2006; Xing et al., 2016), or a combination of the two. The right-shift hypothesis is based on the neural redundancy theory that both hemispheres are capable of supporting speech-motor function (e.g., Schlaug, et al., 2009; Marchina et al., 2018), however, the degree to which this right-hemisphere shift occurs after damage to the left depends upon specific factors (e.g. size, extent, and site of lesions).

Some studies have suggested that right-hemisphere involvement in recovery is actually maladaptive or ineffective (e.g., Belin et al., 1996; Allendorfer et al., 2012). Using voxel-based morphometry, we aimed to test the notion that variation in grey matter density in the right hemisphere is significantly associated with speech outcomes in chronic aphasia, and thus, provide further evidence for beneficial right-shift adaptations.

An initial sample of 49 left-hemisphere stroke patients with aphasia underwent speech assessments using an adapted version of the Western Aphasia Battery and the Boston Naming Test. T1-weighted images were acquired for all patients, and voxel-based morphometry (as implemented in CAT12) was used to determine whether local grey matter density in the right hemisphere explained variance in speech outcomes. The effects of specific treatments (i.e., Melodic Intonation Therapy and Speech Repetition Therapy) on grey matter density were also evaluated in subsamples of the group (n=29) who were assessed before and after 75, 1.5hr therapy sessions.

In the initial sample, Grey Matter density in the right inferior frontal gyrus (Brodmann 47), right middle temporal gyrus, and the temporal pole correlated with scores on the Boston Naming Test (BNT). These findings suggest that right-hemisphere Grey Matter structures can be utilized to support speech-motor function in patients with chronic aphasia. Although it is possible that the premorbid natural development or hypertrophy of these structures facilitate post-stroke aphasia recovery, analysis of the participants who underwent intensive therapy revealed that in one of those structures (Brodmann 47) a significant correlation between grey matter density changes after treatment and changes in BNT performance could be seen, indicating that these right hemisphere Gray Matter differences are indeed the result of intense post-stroke therapy. It is highly probable that intense therapy and practice after a left hemisphere stroke might lead to structural adaptation in right-hemisphere homotopic structures to support speech-motor functions.

## F52: Kinematic Improvement Differs Between Transradial Versus Partial-Hand Prosthesis Use Following Interlimb Training

Emily Keeton, Bennett Alterman, William Hendrix, Jade Lee, Katrina Binkley, Saif Ali, Lewis Wheaton
*Georgia Institute of Technology, Atlanta, USA*

Approaches to improve functional outcomes after upper-limb amputation remain poorly understood. Typically, functional prosthetic limb training cannot begin until the affected limb is healthy enough to be fit with a prosthetic device, allowing more time for compensatory adaptations. However, in unilateral amputees there may be a possibility to enhance prosthesis use by training with a prosthesis simulator on the sound limb before being fit for the device on the affected limb. This approach, interlimb transfer (ILT), may allow for the transfer of learned skills on the trained (non-amputated) limb to the affected limb. Further, level of amputation (proximal or distal) has also been found to affect device acceptance and use due to the distribution of forces along the residuum. This study seeks to evaluate the utility of ILT in improving kinematic and behavioral control of prostheses, and whether there are differences in the effects of ILT between distal (partial-hand) and proximal (transradial) upper-limb prosthesis use. Here, non-amputee participants (n=14) underwent three days of prosthesis training on their non-dominant side between pre-test (day 1) and post-test (day 5) sessions on their dominant side. A control group (n=6) performed only a pre-test (day 1) and follow-up (day 5) test with the prosthesis using their dominant side. Movement duration, accuracy, peak velocity, and variability (coefficient of variation) measures were collected and analyzed for changes in both quantitative and qualitative movement performance. We hypothesized that interlimb training would have a positive effect on prosthesis users of both levels, and partial-hand users will show greater benefit than transradial users. Kinematic and behavioral results found that partial-hand users showed lower movement duration and lower accuracy compared to transradial users. Furthermore, the coefficient of variation of movement duration was also lower in partial-hand compared to transradial prosthesis users. After interlimb training, both transradial and partial-hand prosthesis users exhibited greater performance and stability in movement duration. Not only did the training groups outperform controls in movement duration and stability, but the partial-hand group performed better than the transradial group. During training, partial-hand users showed behavioral improvements in trials completed, trial duration, and errors committed per trial up to 300% greater than those found in transradial users. This work forms the foundation for further examination of ILT for potentially enhancing prosthesis adaptation.

## F53: The Relationship Between Motor and Cognitive Switching During Walking in Stroke Survivors and Age-Matched Healthy Adults

Margaret French, Matthew Cohen, Ryan Pohlig, Darcy Reisman
*University of Delaware, Newark, USA*

### Background:

Motor flexibility is essential for navigating our environment. During an implicit sensorimotor adaptation task, the ability of older adults to switch between walking patterns is related to their cognitive switching ability. However, it remains unclear if this relationship extends to more explicit forms of learning and how neurologic conditions like stroke may affect this relationship. The purpose of this study is to examine 1) the ability of stroke survivors and age-matched healthy adults to switch walking patterns that are learned through an explicit learning task and 2) the relationship between motor and cognitive switching abilities.

### Methods:

Chronic stroke survivors and age-matched healthy adults completed 3 treadmill walking phases: 1) Baseline, 2) Learning, and 3) Normal. During Baseline, step length (SL) was calculated and the leg with the shorter SL was identified (SSL). During Learning, a bar graph representing SL with a target line was displayed in real-time. Subjects were asked to match the bar graph to the target lines; however, the SSL bar was distorted resulting in subjects learning a new walking pattern. During Normal, subjects were instructed to return to their normal walking pattern without visual feedback. Our primary outcome was Switching Index (SI), which is SL of the SSL during Normal minus SL of SSL during Baseline (i.e. how well they returned to their normal walking pattern on command). Subjects also completed the Wisconsin Card Sorting Test (WCST) to measure cognitive switching abilities. Two sequential regressions (healthy and stroke) were completed, with SI as the dependent variable. Age was entered in the first block and number of Perseverative Errors from WCST in the second.

### Results:

Thirteen stroke survivors (65.77 ± 10.13 yrs, 6 F) and thirteen healthy adults (67.54 ± 8.73 yrs, 9 F) participated. During Learning, stroke survivors and healthy adults learned a new walking pattern (both $p<0.001$). During Normal, stroke survivors returned to a pattern that was different from Learning and Baseline ($p<0.001$ and $p=0.017$, respectively). Healthy adults returned to a pattern that was different than Learning ($p<0.001$), but not Baseline ($p=0.052$). In both groups there was variability across subjects in motor switching ability. In stroke survivors, age did not explain this variability ($p=0.361$, $R^2=0.076$), but the addition of WCST did ($p=0.017$, $\Delta R^2=0.263$, $R^2=0.490$). In healthy adults, neither age ($p=0.558$, $R^2= 0.032$) nor WCST explained this variability ($p= 0.082$, $\Delta R^2=0.263$, $R^2=0.295$).

### Discussion:

Our findings show that stroke survivors were not able to return to their baseline walking pattern, suggesting a reduced motor flexibility. Additionally, cognitive switching ability explained a significant portion of variability in stroke survivors but in not healthy adults, suggesting a relationship exists between cognitive and locomotor switching during an explicit learning task in those post-stroke.

## F54: Improvement of TMS Recruitment Curve Data Collection with a Real-Time TMS Display and Analysis System

Margaret Skelly[1], Jessica Mccabe[1], Svetlana Pundik[1,2]
*[1]Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, USA. [2]Case Western Reserve University, Cleveland, USA*

### Purpose:

Pulse transcranial magnetic stimulation (TMS) is used to evaluate cortical spinal excitability by recording motor evoked potentials (MEPs) and estimating a recruitment curve (TMS-rc). A typical TMS-rc recording protocol involves obtaining MEPs at stimulator output levels relative to the motor threshold and fitting a sigmoid curve function offline. Subsequent offline analysis often reveals that there are insufficient data to achieve a good sigmoid curve fit, especially in studies of stroke survivors. Therefore, we developed a real-time data analysis system that displays live EMG activity, shows MEPs from each stimulus, and computes the TMS-rc during a recording session. This real-time analysis ensures that MEP data are collected only when EMG activity is at the desired level and that the appropriate levels of stimuli are applied to obtain sufficient data for a TMS-rc.

### Methods:

A traditional TMS-rc recording protocol consisting of recording MEPs at stimulator output levels of 90, 100, 110, 120, 130, and 150% of motor threshold was compared to the real-time TMS-rc protocol. For the real-time protocol, a Magstim 200[2] TMS stimulator was integrated with a BrainVision Recorder EMG system. Three MATLAB Apps were written to perform the following functions: 1) Stimulator intensity monitoring; 2) EMG activity monitoring with visual feedback display; and 3) TMS-rc sigmoid curve fit analysis. Each TMS stimulus sends a trigger to the EMG recording system that relays it to the Apps. Tibialis anterior muscle TMS-rcs were recorded bilaterally in research participants with chronic motor deficits after stroke. The quality of recruitment curve fit was assessed according to $R^2$ value of the fit to a sigmoid function and the confidence interval of the curve inflection point estimate ($S_{50}$). Fit was considered poor if $R^2 < 0.7$ or the confidence interval of $S_{50}$ exceeded the range of stimulus values recorded. If fit was poor during real time recording, then additional data were obtained to improve the curve fit. Data were recorded and analyzed with both the traditional and real-time methods and reviewed with descriptive statistics.

### Results:

There were 46 TMS-rcs collected from 5 participants using the traditional offline method and 30 TMS-rcs from 6 subjects using the real-time system. Poor curve fit was observed in 46% (21/46) of TMS-rc collected with the traditional offline method and only 17% (5/30) using the real-time method. The number of TMS-rcs that could have been improved with additional (higher or lower) stimulator output levels was 90% (19/21) with the traditional offline analysis method and only 7% (1/15) with the real-time method.

### Conclusion:

Real-time TMS-rc display and analysis is feasible and markedly improved data quality.

### F56: Alteration in Intermuscular Coordination and EMG-EMG Coherence in the Human Upper Extremity After Stroke

Wei Huang, Yunyuan Gao, Jinsook Roh, Yingchun Zhang
*University of Houston, Houston, USA*

Neural control impairments associated with stroke may affect patients' ability to coordinate participating muscles, and consequently impact their motor function negatively. Our previous studies have computationally identified muscle synergies (i.e., consistent muscle co-activation patterns that are flexibly combined to produce complex motor behaviors) and have shown that stroke induces alterations in the synergistic intermuscular coordination in the way that stroke survivors are limited to activate their muscles in isolation in the upper extremity. However, how the muscles identified as a group of synergistically activated ones in a time domain would be modulated in a frequency domain remains unclear. The aim of this study is to test whether the alterations in intermuscular coordination patterns and EMG-EMG coherence are congruent in the upper extremity after stroke. Surface EMG signals of the brachioradialis, biceps brachii, triceps brachii (long and lateral heads), deltoid (anterior, middle, and posterior fibers), and pectoralis major were collected from eight stroke patients and 12 age-matched, neurologically intact individuals during a 3-D isometric force matching task. The 3-D target force space was divided into eight sub-spaces delineated by three mutually perpendicular axes of the Cartesian coordinate system. A non-negative matrix factorization algorithm was applied to the EMG data to identify muscle synergies. Synergistic and non-synergistic muscle pairs were classified based on the results of the muscle synergy analysis. EMG-EMG coherence was calculated with both muscle pairs in control and stroke groups, respectively. A higher coherence was found in synergistic muscle pairs as compared to non-synergistic muscle pairs in both control and stroke groups, respectively. In particular, the anterior and posterior deltoids were identified as temporally synergistic muscles in the synergy analysis in stroke only, and the EMG-EMG coherence of the anterior and posterior deltoids was significant in stroke but not in the control group. Across the eight sub-spaces, no significant difference was found in the results of the coherence analysis. Overall, these results suggest that the alteration in intermuscular coordination and EMG-EMG coherence after stroke may provide congruent and complementary information about how stroke affects intermuscular coordination in the human upper extremity.

## F57: Using TMS to Inform Paradigms of DBS in Human Stroke Motor Recovery

Kyle O'Laughlin[1], Ela Plow[1], Tarun Arora[1], Alexandria Wyant[1], Kelsey Potter-Baker[2], Yin-Liang Lin[3], Raghavan Gopalakrishnan[1], Darlene Floden[1], Kenneth Baker[1], Andre Machado[1]
[1]*Cleveland Clinic, Cleveland, USA.* [2]*University of Texas, Rio Grande Valley, USA.* [3]*Natl. Yang-Ming Univ., Taipei, Taiwan*

Brain stimulation is a promising experimental technique to promote upper limb motor recovery following stroke but outcomes achieved in severe patients have been limited. Typically, brain stimulation is delivered to facilitate the activity of residual motor cortices in hopes of promoting contribution of perilesional motor areas to upper limb movement. But this approach tends to fail when the damage to targeted motor cortical regions and emergent corticospinal pathways is extensive. Our group is investigating whether a new approach of targeting the dentatothalamocortical pathways at their origin using invasive, deep brain stimulation (DBS) could enhance outcomes via spared cerebellar projections to widespread cortical regions. This translational effort is supported by more than a decade of preclinical work showing that dentate DBS induces positive therapeutic benefits in ischemic stroke models in association with gains in motor cortical excitability, synaptogenesis and functional re-mapping (Cooperrider et al., 2014 *J Neurosci*). Six patients (<2yrs post-stroke) with severe motor impairment (Fugl-Meyer (FM) < 33) have received DBS in conjunction with rehabilitation for 4 months after reaching a plateau in motor performance with rehabilitation alone. Assessment of motor impairment (FM) and neurophysiology is completed at many time-points before, during and after DBS + Rehab. Neurophysiology is tested using a non-invasive brain stimulation technique- Transcranial Magnetic Stimulation (TMS). TMS is being paired with DBS for the first time to 1) guide patient selection through pre-surgical confirmation of corticospinal pathway viability – a key predictor of therapeutic-response, 2) inform DBS programming by measuring acute, DBS-induced changes in motor cortical excitability, and 3) characterize changes in cortical excitability and remapping of motor networks as a function of treatment-related gains. In association with gains in FM, our findings reveal acute facilitatory effects of dentate DBS on *ongoing*motor cortical activity measured with TMS at short-latencies (2ms-5ms), consistent with the fast, disynaptic nature of dentatothalamocortical connections (acute 30Hz DBS ON vs. OFF, p= 0.03). TMS also reveals similar gains in motor cortical excitability and functional re-mapping as witnessed previously in animal studies (6% to 26% reduction in TMS current required and 5- to 8-point gain in number of motor cortical sites producing criterion response in weak muscles). These data indicate that targeting dentatothalamocortical connections after severe stroke facilitates perilesional as well as contralesional motor cortical activity and opens an opportunity for generating dynamic understanding of underlying mechanisms.

## F58: Subventricular Zone-derived Neural Precursor Cells Support Tissue Remodeling After Ischemic Cortical Lesions

***2019 Presidential Award Recipient***

Michael Williamson, Stephanie Le, Ronald Franzen, Andrew Dunn, Michael Drew, Theresa Jones
*University of Texas at Austin, Austin, USA*

Stroke and other brain injuries cause proliferation and ectopic migration of neural precursor cells (NPCs) from the subventricular zone (SVZ) towards the site of injury. Contributions to recovery of this cytogenic response remain unclear. Using an indelible lineage tracing system, we found that photothrombotic ischemic lesions in mouse sensorimotor cortex prompted a multi-lineage migratory response; new astrocytes, neurons, and oligodendrocytes arose from SVZ-derived NPCs and localized in peri-infarct cortex. Surprisingly, at two weeks post-infarct the large majority of SVZ-derived cells in peri-cortex expressed Sox2—a marker of multipotency—suggesting that either most SVZ-derived cells remain undifferentiated or that they proliferate locally within the injury-created ectopic niche. In vivo two-photon imaging revealed that SVZ-derived NPCs in peri-infarct cortex often extend thin processes that contact nearby blood vessels. To evaluate whether NPCs influence the vascular remodeling response to injury we conditionally ablated NPCs in the adult brain of GFAP-thymidine kinase mice prior to motor cortical infarcts. Total vessel density in peri-infarct cortex of mice lacking NPCs was increased relative to mice with intact NPCs. By contrast, the density of perfused vessels in peri-infarct cortex was diminished in mice lacking NPCs. Longitudinal multi-exposure speckle imaging of cortical surface blood flow revealed that re-establishment of peri-infarct blood flow was delayed in mice lacking NPCs. Therefore, NPCs support effective vascular structural remodeling and recovery of blood flow surrounding ischemic lesions. We also monitored time- and space-resolved synaptic remodeling in superficial peri-infarct cortex with two-photon imaging of fluorescently labeled pyramidal neurons to examine whether neuronal remodeling is influenced by NPCs. Importantly, ablation of NPCs prior to motor cortical infarcts worsened recovery of skilled motor function on the single seed reaching task. Our results indicate that SVZ-derived NPCs support tissue remodeling and behavioral recovery after focal ischemic brain injury.