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Oral Session

O1: Spontaneous Motor Recovery After Cerebrolysin Treatment in a Mouse Model of Stroke

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Background and Purpose: Most functional upper extremity motor recovery occurs in the first 4 weeks after ischemic stroke in humans and in the first week in rodent models. The majority of functional recovery in humans is spontaneous (ie, occurs as a result of endogenous repair processes rather than rehabilitative interventions). In mouse models of stroke, recovery is impaired when poststroke rehabilitation is delayed and there is very little spontaneous recovery. Cerebrolysin is a polypeptide preparation shown to enhance neuronal plasticity and to promote motor recovery in patients after stroke. In mice, we tested the hypothesis that Cerebrolysin can act early after stroke to enhance spontaneous motor recovery.

Methods: Adult C57Bl/6 mice were trained to perform a skilled prehension task to an asymptotic level of performance, after which they underwent photocoagulation-induced stroke in the caudal forelimb area (rodent primary motor cortex). The mice were then randomized to receive Cerebrolysin or saline injections beginning either after 1 day or 7 day poststroke delay. Animals were then retrained at the same prehension task by a blinded investigator. Stroke volumes were compared using immunohistochemistry.

Results: We have previously shown that training-associated recovery of prehension is complete if training is initiated after a 1-day delay but incomplete if training is initiated after a 7-day delay, even with additional training days. However, daily Cerebrolysin administration beginning after a 1-day poststroke delay was associated with complete recovery of prehension by day 8, even in the absence of training. To test if delayed Cerebrolysin administration could recover poststroke prehension, even when started days later, we administered daily IP injections of either Cerebrolysin or saline beginning 7 days poststroke. Animals receiving Cerebrolysin displayed improved motor recovery even though both Cerebrolysin administration and rehabilitative training were delayed by 7 days and 8 days, respectively. Stroke volumes were similar across all groups.

Conclusions: We conclude that Cerebrolysin administration can lead to recovery of motor function, even in the absence of motor training. This is one of the first demonstrations of spontaneous motor recovery in a rodent stroke model. Our mouse model, with all of the attendant genetic benefits, should allow us to determine at the cellular and molecular levels how endogenous plasticity and medications like Cerebrolysin interact to mediate recovery.

O2: Effect of Behavioral Practice Targeted at the Premotor-Prefrontal Component of the Motor Network After Stroke

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Introduction: Changes in task conditions lead to changes in neural activation that are condition-specific, providing an avenue for creating behavioral practice conditions that target a specific component of the motor network. The addition of action selection demands to movement through abstract, visual cues engages dorsal premotor cortex (PMd). After stroke, bilateral PMd and dorsolateral prefrontal cortices (DLPFC) show changes in activation and connectivity in response to action selection demands; however, the plasticity of this component of the motor network with practice is unknown. The purpose of this study was to determine the response to a period of practice targeted at the PMd-DLPFC component of the motor network after stroke.

Methods: Seventeen individuals poststroke (age: 57.4 ± 10.1 years; months poststroke: 41.9 ± 41.7 ; UE FM motor score: 43.8 ± 15.4) completed a task that required right or left movement of a joystick with the weaker hand under 2 conditions. In the Execute condition, the individual moved the same direction on every trial. In the Select condition, the individual moved right or left based on an abstract, visual rule. The task was practiced for 4 consecutive days and completed during functional magnetic resonance imaging on days 1 and 4.

Results: On day 1, reaction time (RT) was longer in Select (1.158 ± 0.365 seconds) compared to Execute (0.554 ± 0.201 seconds). This increase in RT during Select corresponded to increased activation in bilateral PMd as well as bilateral DLPFC, supplementary motor area, anterior cingulate and parietal cortices. Over days of practice, Select RT and RT cost (Select RT-Execute RT; represents the relative increase in planning time for the Select condition) decreased ($P = .002$; RT cost: day 1 0.604 ± 0.235 ; day 4 0.360 ± 0.101). On day 4, the increase in brain activation from the Execute to the Select condition was overall less including in bilateral DLPFC, ipsilateral PMd, and anterior cingulate cortex. No behavioral or brain activation changes were seen with Execute. PMd-M1 and PMd-DLPFC connectivity changed with practice but the direction of change varied, with some individuals showing an increase in connectivity ($n = 9$) and others showing a decrease ($n = 8$). Brain-behavior relationships also changed with practice: on day 1, PMd activation had a negative relationship with RT cost ($r = -0.594$) such that individuals with relatively worse performance (higher cost) had lower activation in PMd, while on day 4, this relationship became positive such that individuals with relatively worse performance had higher activation in PMd ($r = 0.476$) and DLPFC ($r = 0.492$).

Conclusion: Behavioral practice targeted at the premotor-prefrontal component of the motor network can change the activation pattern in task-related regions. Changes in brain-behavior relationships over practice

were recruitment rate, successful protocol completion, and documentation of safety incidences. Additionally, preliminary data on BLT training efficacy (step length, cadence, symmetry) and change in over-ground walking performance (10-meter walk test), and exercise capacity (6-minute walk test) were collected at baseline, posttraining, and at 1 month. Enrollment goal is 36 participants.

Results: Between September 5, 2017, through July 10, 2018, 25 people were screened, and 21 met the criteria for enrollment. Ninety-five percent (20 of 21) enrolled participants successfully completed the study. One dropout occurred on day 1 of 6 of training and was due to excess fatigue. There were no serious adverse events with BLT or tsDCS, and both were well tolerated. All patients reported feeling stronger and more confident in forwarding walking. Posttraining, the mean change in walking speed was $+0.27 \pm 0.20$ m/s and sustained $+0.30 \pm 0.21$ m/s at 1 month. Similarly, there was a 56.2 ± 38.8 M improvement in walking capacity posttraining and 65.5 ± 41.0 M at 1 month.

Conclusion: This pilot study shows the feasibility and safety of BLT + tsDCS in stroke. Our preliminary findings suggest that our BLT protocol is efficacious in improving over-ground walking speed and exercise capacity in chronic stroke patients. To maintain blinding, between-group comparison (to determine the effect of tsDCS) is deferred until study completion.

F50: A Novel EMG-Based Robotic Control for Restoring Normal Synergies After Stroke

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Muscle weakness and loss of independent joint control are the 2 most common neuromotor impairments after stroke. While there are a number of approaches to improve poststroke muscle weakness, there are currently no rehabilitation strategies that directly target a patient's inability to match and independently activate the normal patterned muscle coordination strategies, or "muscle synergies." Our goal is to develop an EMG-based controller for retraining healthy muscle synergies in patients with stroke-related disabilities. The controller can be integrated into rehabilitation robots for their ability to structure the robot's force output based on input EMG activity. However, developing such a controller would require a clear understanding of the relationship between the applied force from a rehabilitation robot and the resulting changes to a patient's muscle synergies. Therefore, this study was performed to quantify how the muscle synergies of horizontal planar-reaching are affected by direction of an applied force at the end-effector (ie, hand). A 2 DOF, 10 muscle model was developed in MATLAB using parameters obtained from the OpenSim (version 3.3) open source software system. Simulation experiments were then performed in MATLAB to investigate the relationship between the applied force and the resulting muscle synergies. The simulated event was composed of several trials of the same right-handed, planar, multidirectional reaching task from 0° (to the right) to 360°. Each trial applied a different steering force direction at the subject's hand, varying from -45° to 45° relative to the reaching direction. The simulation trials were also validated by evaluating the EMG patterns of a healthy subject when performing the same reaching task with varying steering force directions. For the 0° steering force trials, the muscle synergies and their activation timings were extracted using nonnegative matrix factorization (NMF). For all other trials, the synergy matrix was fixed and the activation timings were extracted from the product of the EMG of that trial and the pseudo-inverse of the synergy matrix from the 0° steering force trial. By fixing the synergy matrix in the trials with

steering forces, we can directly track activation changes of a certain synergy as steering force is varied. For both simulation and experimental trials, circular statistics revealed a linear relationship between changes in steering force direction and principal direction of synergy activation. These results suggest that the activation of a synergy can be controlled directly by the direction of an applied steering force. This has relevant implications in synergy-based controller design because a computer can easily manipulate a patient's muscle synergies and track the changes while avoiding the computational expense of NMF. In addition, similar analysis could be used to extract the relationship between applied forces and changes in synergies for other types of motion.

F51: Validity of Subjective Sleep Inventories for Assessment of Sleepiness in Inpatient Rehabilitation for Stroke

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Objective: To study the association between self-report measures of sleepiness and sensor-based objective sleep measures among patients with stroke during inpatient medical rehabilitation.

Design: Patients receiving inpatient rehabilitation for stroke were consecutively approached to participate. Participants were fitted with an actigraph for 4 days and administered 3 subjective measures of sleepiness: Karolinska Sleepiness Scale (KSS), Wits Pictorial Sleepiness Scale (WPSS), and a Fatigue Visual Analog Scale (VAS) on days 2 and 4. Objective sleep metrics derived from the actigraph were minutes of nighttime sleep and minutes of daytime sleep. **Setting:** Inpatient rehabilitation facility. **Participants:** Adult male and female patients receiving inpatient rehabilitation services for stroke. **Interventions:** None. **Main Outcome Measures:** KSS, WPSS, VAS, minutes of nighttime sleep, and minutes of daytime sleep.

Results: Correlations as measures of criterion-related validity were derived among subjective and objective sleep measures on 16 patients with stroke. The only correlations that were significant were among the KSS and minutes of daytime sleep (r range = .522 to .556). No subjective measures correlated with nighttime sleep (r range = -.472 to .324).

Conclusions: There was poor agreement between subjective measures of nighttime sleep and objective metrics of sleep, suggesting that self-report sleep measures may not accurately represent true sleep status in stroke. The KSS seems to be effective for identifying patients with excessive daytime sleep. Further work is needed to identify subjective sleepiness scales for use in patients with stroke.

F52: Interventions to Augment Upper Extremity Motor Improvement in Individuals With a Traumatic Brain Injury: A Systematic Review

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