STROKE RECOVERY RESEARCH CENTER

A Center of Biomedical Research Excellence (COBRE) in Stroke Recovery at the Medical University of South Carolina

CHANGING THE FACE OF RESEARCH

COBRE STRATEGIC MEETING

COBRE news and updates discussed at the Strategic Meeting in October of 2019. What does COBRE's future look like?

More on Page 3

COBRE PI PUBLICATIONS

COBRE's Principal Investigators are always working hard, whether it's within the SRRC or not. See some of their newer 2019 publications.

More on page 7-9

RESTORE UPDATES

Find out new and exciting RESTORE updates.

More on Page 10

FROM THE DIRECTOR

Reprinted below are the Director's comments from COBRE PHASE II CEREMONY in June, 2019

Good afternoon. It is so nice to be with you today and see so many familiar faces – those who have helped the COBRE get to where we are today. This includes all of those wearing the blue Stroke Recovery Research Center shirts, who include our scientists and our amazing research staff.

Our mission is to enable translational research into neural recovery from stroke in order to provide clinicians with optimal tools for diagnosing and treating individuals, because we want to improve the recovery and long-term quality of life of those who have survived a stroke. We serve two distinct groups, both of who have helped tremendously with the success of COBRE.

First and foremost, we exist to serve those who have survived a stroke and for whom our science can have real impact. As you know, stroke is one of the most debilitating conditions in the United States with limited treatment options – and South Carolina is in the buckle of the Stroke Belt. One-in-fifty of the 7 million stroke survivors across the country live in South Carolina. Each year, stroke-related expenses total more than $1 billion per year in South Carolina.

Second, we also serve the scientists at MUSC and especially the more junior researchers who will be the future leaders in this field. We were charged to build a world class research center here at MUSC – and that only happens by providing the infrastructure to allow MUSC researchers to grow and flourish – Phase I has been extraordinary, and Phase II will build upon this foundation.

I'm very glad to have Dr. Robert Adams as my Associate Program Director. Dr. Adams is the SmartState Endowed Chair in Stroke in the College of Medicine. I am also extremely grateful to have Drs. Mark George and Truman Brown as our other core leaders. I also would like to thank our institutional leaders for their support and commitment – Drs. Cole, Saladin, Kapasi, Brady and Mark Sothmann.

Phase I of the grant has been incredibly successful. The number of stroke recovery researchers increased from 9 pre-COBRE award to 27 during Phase I. These investigators have successfully competed for more than $43 Million in grant awards. All 5 COBRE-supported junior faculty have launched successful independent research careers with more than $17 Million in grant awards from NIH and the US Department of Veterans Affairs. Over 1,000 participants have consented to take part in research studies, with 120+ publications generated from research activities.

Recognition of the center's extraordinary achievements and unique environment was demonstrated by award of a rehabilitation research infrastructure center grant from the NIH, one of only six in the nation – the National Center of Neuromodulation for Rehabilitation (NM4R). The NM4R makes training and resources developed in the COBRE available nationwide and puts COBRE researchers in the forefront of the field of neuromodulation. In April 2019, MUSC and the College of Health Professions hosted an international conference dedicated to neuromodulation; and earlier this month, our research center was visited by the US Secretary of Veterans Affairs.

Most importantly, we have overcome all of the usual barriers to multidisciplinary research and created a cohesive team of College of Health Professions and College of Medicine researchers working together to produce significant achievements in the field of stroke recovery. I believe the coming years will be even more productive as the seeds planted in Phase I will reach the point of maturity in Phase II. We will continue to launch independent research careers in stroke recovery and grow the number of clinical trials in stroke recovery. We will become leaders in archiving stroke recovery research data for use by investigators and international teams. And finally, we will plan for an independent and sustainable, multidisciplinary stroke recovery research program at the end of COBRE funding.

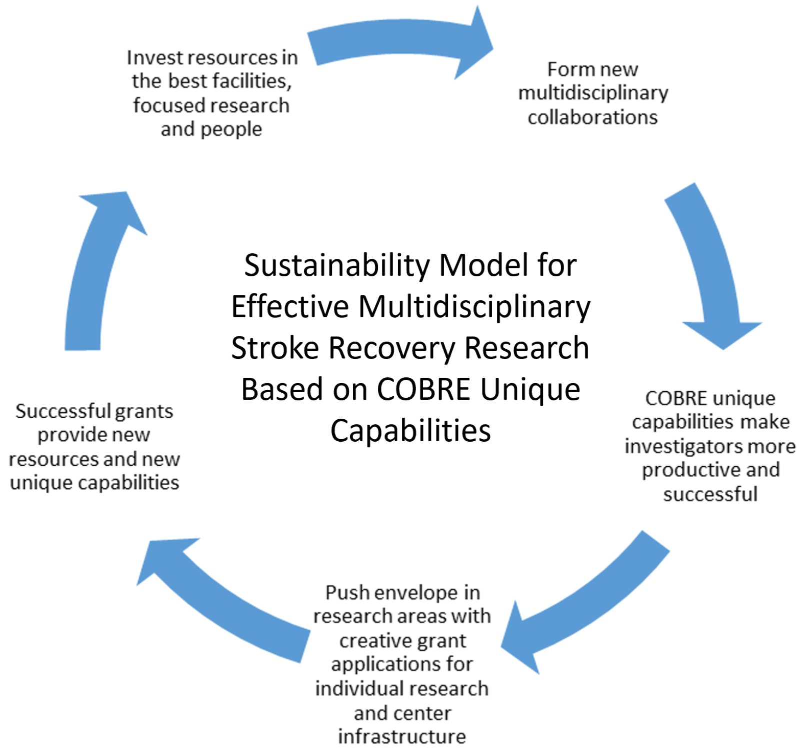
I am asking for all of your support. To achieve all that we want to achieve it will take the whole community – our participants, our scientists, our great research staff, and the support of our institutional leaders and our donors.

- Steve Kautz, Ph.D.

Steve Kautz, Ph.D.

Director of the Stroke Recovery Research Center

COBRE Strategic Planning Meeting
October 2019



What are the unique capabilities that sets the COBRE in Stroke Recovery apart?

1. Processes and resources that make life easier and increase productivity of all COBRE investigators.

2. Combine insights from multiple disciplines and systems through team meetings and collaborations.

3. Provide easy inclusion of advanced technology and measurement from multiple disciplines and systems into grant applications.

4. Synthesize results into an interdisciplinary database for maximal data reuse and sharing.

MEET THE EDITOR

“My name is Brenna and I am the new program coordinator for COBRE and NM4R. I recently graduated from UNC Greensboro in May and completed a year internship at The National Crime and Victims Center at the Institute of Psychiatry here at MUSC. I currently have my Bachelor of Science in Public Health and plan on beginning my Masters in Public Health sometime next year. Before working at MUSC, I was a medical massage therapist for over 11 years so rehabilitation has always been a passion of mine.

A little peek into my personal life; I have two big dogs, one special needs 85lbs long-coat Akita (Woolie) and one 95lbs Pitbull/Rottweiler mix. They are both rescues from the Carolinas. I’m also a millennial wanderlust and love traveling around the world. I got engaged in Japan, married in Mexico, and honeymooned in Cuba. Our next adventure will be spending two weeks in Thailand and Vietnam in March of 2020.

I am extremely excited to be a part of The Stroke Recovery and Research Center and COBRE team here at MUSC.”

Brenna Baker-Vogel

COBRE & NM4R
Program Coordinator

WELCOME THE NEW COBRE TEAM MEMBERS

“My name is Jamie and I was born and raised in Charleston, SC. I received a B.S. in Biology from the College of Charleston and a B.S. in Mechanical Engineering from The Citadel. As a Systems Engineer, I provide engineering support for research studies focusing on neurorehabilitation and lower extremity movement. This includes collecting data and developing, fabricating, and programming devices specific to the needs of each research study. My goal is to be able to independently provide engineering solutions for the COBRE investigators that throttle the research studies.”

Jamie Rodriguez
Systems Engineer

“My name is Changki and I am a new postdoctoral associate here at the SRRC. I started working with Dr. Na Jin Seo in August of 2019. My research interests span motor control and neuromuscular physiology. During my PhD training, my research focused on the effects of visual information processing on motor control in aged-population, and demonstrated underlying neuromuscular mechanisms using surface EMG. During my first postdoc, I focused on characterizing neural control in different hand motor tasks using motor unit decomposition technique. Findings and experience during the trainings led me to question motor control in stroke populations and rehabilitation. I am excited to be a part of the COBRE team here at MUSC.”

Changki Kim, Ph.D.
Postdoctoral Associate

COBRE Junior PI Highlight

Dr. Badran is a neuroscientist junior investigator that has developed transcutaneous auricular vagus nerve stimulation (taVNS) here at MUSC since 2013. After completing a series of parametric optimization studies, he is now moving the technology into the clinic, where he is investigating the use of taVNS for neuropsychiatric disorders. Dr. Badran currently has two active COBRE/NM4R funded studies:

Motor-Activated Auricular Vagus Nerve Stimulation (MAAVNS) to enhance upper limb function post-stroke- We have developed a noninvasive form of VNS known as transcutaneous auricular VNS (taVNS). For paired taVNS to succeed as a clinical treatment, it is critical to develop and refine a closed-loop taVNS platform that delivers stimulation concurrently during specific movements of the motor rehabilitation training. Aim 1 develops this novel motor-activated closed-loop system that delivers taVNS in synchrony with specific upper limb motor activation.

Boosting motor cortex excitability by combining repetitive transcranial magnetic stimulation (rTMS) with transcutaneous auricular vagus nerve stimulation- There is a new noninvasive form of brain stimulation known as transcutaneous auricular vagus nerve stimulation (taVNS) which may facilitate plasticity and is being investigated in the enhancement of motor learning and recovery in a specific paired fashion. The timing of the paired VNS is critical to the desired neuroplastic changes as the behavioral effects of paired therapy disappear when behavior is not intricately synchronized with stimulation. Could pairing taVNS with TMS boost the effects of TMS on cortex, and potentially emerge as a stroke recovery tool? As a first step in this direction, we are conducting a mechanistic pilot study exploring the use of paired taVNS/TMS to further enhance motor cortex excitability.

Bashar Badran, Ph.D.
Assistant Professor
Department of Psychiatry and Behavioral Sciences

Dr. Robinson's lab focuses on understanding the impact of metabolic disorders on both normal and pathological brain aging. Her lab is particularly interested in the impact of diet-induced metabolic risk factors on cognitive function, Alzheimer's disease onset and progression, and stroke recovery. Metabolic risk factors such as diabetes, obesity, insulin resistance, and high cholesterol alters brain function and has negative consequences on learning and memory. These factors likely induce changes in various pathways years prior to any noticeable symptom. Hence, the goal of her laboratory is to identify these early changes in order to develop novel therapeutic targets to delay or prevent disease progression.

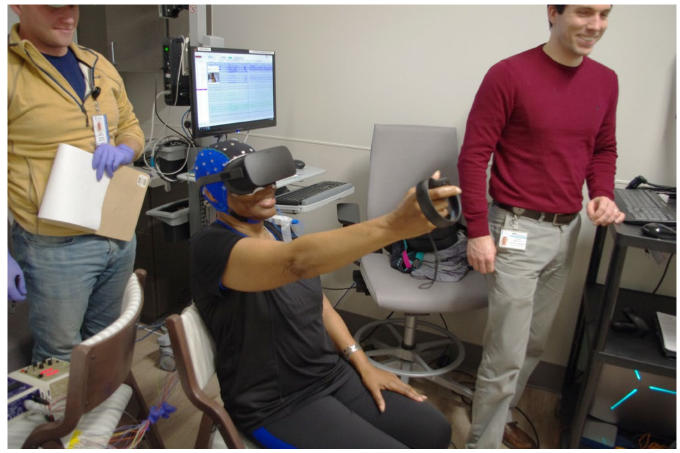
Dr. Robinson's COBRE study, "Effects of insulin on neuroplasticity and cognitive rehabilitation". Insulin resistance, which is a common comorbidity among stroke survivors, leads to a deficiency of insulin in the brain. Brain insulin promotes neuroplasticity, synaptogenesis, has anti-inflammatory, anti-thrombotic, vasodilatory, anti-apoptotic properties, and is involved in cognition. Hence, the goal of this project is to investigate the role of reduced brain insulin and the therapeutic potential of intranasal insulin on long-term functional stroke recovery.

Catrina Robinson, Ph.D.
Assistant Professor
Department of Neurology

COBRE Study Highlight

Effect of tdcs on cortical oscillations during a VR task

Dr. Nathan Rowland



Over 6.5 million individuals in the US suffer from chronic stroke, however no standard therapeutic options for neuromodulation currently exist for this group. In contrast, much rarer forms of motor dysfunction, such as Parkinson's disease (PD, ~ 1 million diagnosed in the US), benefit from diverse neuromodulatory techniques, including invasive (e.g., deep brain stimulation, DBS) and noninvasive (e.g., MRI-guided focused ultrasound) approaches. Transcranial direct current stimulation (tDCS), a noninvasive form of neuromodulation, has shown potential to improve motor deficits following chronic stroke, however a detailed understanding of motor cortical response to tDCS is lacking. To address this problem, in a parallel IRB-approved study (Pro00073545), we have used tDCS in subjects with movement disorders undergoing DBS surgery to understand its effects on motor cortical oscillations.

In the current proposal, we will expand our investigation of tDCS effects on subjects with chronic stroke using noninvasive electroencephalographic (EEG) recordings. In this proposal, we also plan to recruit healthy controls as well as patients with movement disorders. All prospective participants will be recruited from databases in which patients have previously given consent to be contacted about future research studies such as this one. We will use two databases: the chronic stroke patients (n=20) and healthy controls (n=10) will be recruited from the Registry for Stroke Recovery (RESTORE) database; the movement disorders patients (n=10) will be recruited from the MUSC Movement Disorders Program patient database. This will allow us to compare cortical effects of tDCS between invasive and noninvasive approaches and determine how these signals might be used in future neuromodulation strategies for improving recovery in chronic stroke patients.

Aim 1**.** Quantify the change in primary motor cortical (PriMC) oscillations during cued arm reaching in relation to anodal tDCS activation. Question: Does tDCS differentially modulate movement preparation vs movement execution? In this aim, we will record beta and broadband gamma activity in PriMC in subjects undergoing EEG recording and high-density tDCS. *We hypothesize that cortical beta and broadband gamma spectral power changes will be enhanced more so during movement preparation than execution following anodal tDCS activation.*

Aim 2. Quantify the change in PriMC oscillations during motor imagery in relation to anodal tDCS activation. Question: Does tDCS differentially modulate motor imagery of simple vs complex movements? Using the same subjects as Aim 1, cortical oscillatory changes will be recorded during imagery of arm flexion/extension (simple) versus randomly chosen variants of arm flexion/extension (complex). *We hypothesize that cortical beta and broadband gamma spectral power changes will be enhanced more so during complex arm flexion/extension than simple arm flexion/extension following anodal tDCS activation.*

2019 COBRE Publications

Badran, B. W., Ly, M., DeVries, W. H., Glusman, C. E., Willis, A., Pridmore, S., & George, M. S. (2019). Are EMG and visual observation comparable in determining resting motor threshold? A reexamination after twenty years. Brain Stimul, 12(2), 364-366. doi:10.1016/j.brs.2018.11.003

Badran, B. W., Yu, A. B., Adair, D., Mappin, G., DeVries, W. H., Jenkins, D. D., . . . Bikson, M. (2019). Laboratory Administration of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS): Technique, Targeting, and Considerations. J Vis Exp(143). doi:10.3791/58984

Brough, L. G., Kautz, S. A., Bowden, M. G., Gregory, C. M., & Neptune, R. R. (2019). Merged plantarflexor muscle activity is predictive of poor walking performance in post-stroke hemiparetic subjects. J Biomech, 82, 361-367. doi:10.1016/j.jbiomech.2018.11.011

Campagnoli, R. R., Wieser, M. J., Gruss, L. F., Boylan, M. R., McTeague, L. M., & Keil, A. (2019). How the visual brain detects emotional changes in facial expressions: Evidence from driven and intrinsic brain oscillations. Cortex, 111, 35-50. doi:10.1016/j.cortex.2018.10.006

Charalambous, C. C., Liang, J. N., Kautz, S. A., George, M. S., & Bowden, M. G. (2019). Bilateral Assessment of the Corticospinal Pathways of the Ankle Muscles Using Navigated Transcranial Magnetic Stimulation. J Vis Exp(144). doi:10.3791/58944

Dean, J. C., Bowden, M. G., Kelly, A. L., & Kautz, S. A. (2019). Altered post-stroke propulsion is related to paretic swing phase kinematics. Clin Biomech (Bristol, Avon), 72, 24-30. doi:10.1016/j.clinbiomech.2019.11.024

Fridriksson, J., Basilakos, A., Stark, B. C., Rorden, C., Elm, J., Gottfried, M., . . . Bonilha, L. (2019). Transcranial direct current stimulation to treat aphasia: Longitudinal analysis of a randomized controlled trial. Brain Stimul, 12(1), 190-191. doi:10.1016/j.brs.2018.09.016

Grattan, E. S., Velozo, C. A., Skidmore, E. R., Page, S. J., & Woodbury, M. L. (2019). Interpreting Action Research Arm Test Assessment Scores to Plan Treatment. OTJR (Thorofare N J), 39(1), 64-73. doi:10.1177/1539449218757740

Johnson, L., Basilakos, A., Yourganov, G., Cai, B., Bonilha, L., Rorden, C., & Fridriksson, J. (2019). Progression of Aphasia Severity in the Chronic Stages of Stroke. Am J Speech Lang Pathol, 28(2), 639-649. doi:10.1044/2018_ajslp-18-0123

Kindred, J. H., Kautz, S. A., Wonsetler, E. C., & Bowden, M. G. (2019). Single Sessions of High-Definition Transcranial Direct Current Stimulation Do Not Alter Lower Extremity Biomechanical or Corticomotor Response Variables Post-stroke. Front Neurosci, 13, 286. doi:10.3389/fnins.2019.00286

Roelker, S. A., Bowden, M. G., Kautz, S. A., & Neptune, R. R. (2019). Paretic propulsion as a measure of walking performance and functional motor recovery post-stroke: A review. Gait Posture, 68, 6-14. doi:10.1016/j.gaitpost.2018.10.027

Roelker, S. A., Kautz, S. A., & Neptune, R. R. (2019). Muscle contributions to mediolateral and anteroposterior foot placement during walking. J Biomech, 95, 109310. doi:10.1016/j.jbiomech.2019.08.004

Seo, N. J., Enders, L. R., Fortune, A., Cain, S., Vatinno, A. A., Schuster, E., . . . Feng, W. (2019). Phase I Safety Trial: Extended Daily Peripheral Sensory Stimulation Using a Wrist-Worn Vibrator in Stroke Survivors. Transl Stroke Res. doi:10.1007/s12975-019-00724-9

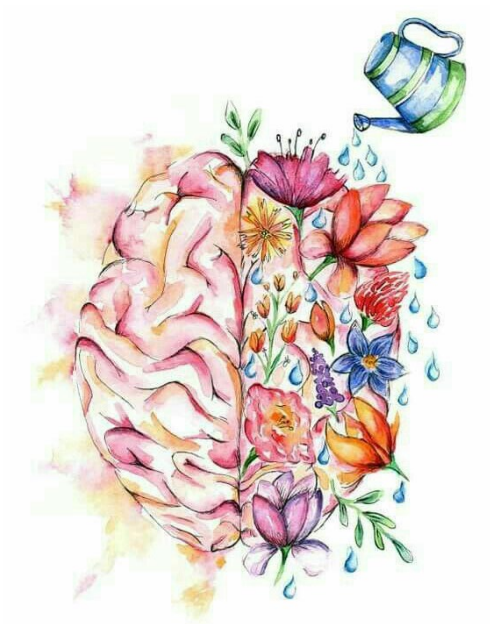
Seo, N. J., Lakshminarayanan, K., Lauer, A. W., Ramakrishnan, V., Schmit, B. D., Hanlon, C. A., . . . Nagy, T. (2019). Use of imperceptible wrist vibration to modulate sensorimotor cortical activity. Exp Brain Res, 237(3), 805-816. doi:10.1007/s00221-018-05465-z

Seo, N. J., Woodbury, M. L., Bonilha, L., Ramakrishnan, V., Kautz, S. A., Downey, R. J., . . . Vatinno, A. A. (2019). TheraBracelet Stimulation During Task-Practice Therapy to Improve Upper Extremity Function After Stroke: A Pilot Randomized Controlled Study. Phys Ther, 99(3), 319-328. doi:10.1093/ptj/pzy143

Srivastava, S., Patten, C., & Kautz, S. A. (2019). Altered muscle activation patterns (AMAP): an analytical tool to compare muscle activity patterns of hemiparetic gait with a normative profile. J Neuroeng Rehabil, 16(1), 21. doi:10.1186/s12984-019-0487-y

Vistamehr, A., Kautz, S. A., Bowden, M. G., & Neptune, R. R. (2019). The influence of locomotor training on dynamic balance during steady-state walking post-stroke. J Biomech, 89, 21-27. doi:10.1016/j.jbiomech.2019.04.002

Wilmskoetter, J., Bonilha, L., Martin-Harris, B., Elm, J. J., Horn, J., & Bonilha, H. S. (2019). Mapping acute lesion locations to physiological swallow impairments after stroke. Neuroimage Clin, 22, 101685. doi:10.1016/j.nicl.2019.101685



"Keep going, keep growing."

-Patty

Single Sessions of High-Definition Transcranial Direct Current Stimulation Do Not Alter Lower Extremity Biomechanical or Corticomotor Response Variables Post-stroke.

Kindred, John H., Kautz, Steve A., Wonsetler EC, Bowden, Mark G.

Abstract:

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique used to modulate cortical activity. However, measured effects on clinically relevant assessments have been inconsistent, possibly due to the non-focal dispersion of current from traditional two electrode configurations. High-definition (HD)-tDCS uses a small array of electrodes (N = 5) to improve targeted current delivery. The purpose of this study was to determine the effects of a single session of anodal and cathodal HD-tDCS on gait kinematics and kinetics and the corticomotor response to transcranial magnetic stimulation (TMS) in individuals post-stroke. We hypothesized that ipsilesional anodal stimulation would increase the corticomotor response to TMS leading to beneficial changes in gait. Eighteen participants post-stroke (average age: 64.8 years, SD: 12.5; average months post-stroke: 54, SD: 42; average lower extremity Fugl-Meyer score: 26, SD: 6) underwent biomechanical and corticomotor response testing on three separate occasions prior to and after HD-tDCS stimulation. In a randomized order, anodal, cathodal, and sham HD-tDCS were applied to the ipsilesional motor cortex for 20 min while participants pedaled on a recumbent cycle ergometer. Gait kinetic and kinematic data were collected while walking on an instrumented split-belt treadmill with motion capture. The corticomotor response of the paretic and non-paretic tibialis anterior (TA) muscles were measured using neuronavigated TMS. Repeated measures ANOVAs using within-subject factors of time point (pre, post) and stimulation type (sham, anodal, cathodal) were used to compare effects of HD-tDCS stimulation on measured variables. HD-tDCS had no effect on over ground walking speed ($P > 0.41$), or kinematic variables ($P > 0.54$). The corticomotor responses of the TA muscles were also unaffected by HD-tDCS (resting motor threshold, $P = 0.15$; motor evoked potential (MEP) amplitude, $P = 0.25$; MEP normalized latency, $P = 0.66$). A single session of anodal or cathodal HD-tDCS delivered to a standardized ipsilesional area of the motor cortex does not appear to alter gait kinematics or corticomotor response post-stroke. Repeated sessions and individualized delivery of HD-tDCS may be required to induce beneficial plastic effects. Contralesional stimulation should also be investigated due to the altered interactions between the cerebral hemispheres post-stroke.

Capturing Upper Limb Gross Motor Categories Using the Kinect® Sensor.

Seo, Na Jin, Crocher, Vincent, Spaho, Egli, Ewert, Charles R., Fathi, Mojtaba F., Hur, Pilwon, Lum, Sarah A., Humanitzki, Elizabeth M., Kelly, Abigail L., Ramakrishnan, Viswanathan, Woodbury, Michelle L.

Abstract:

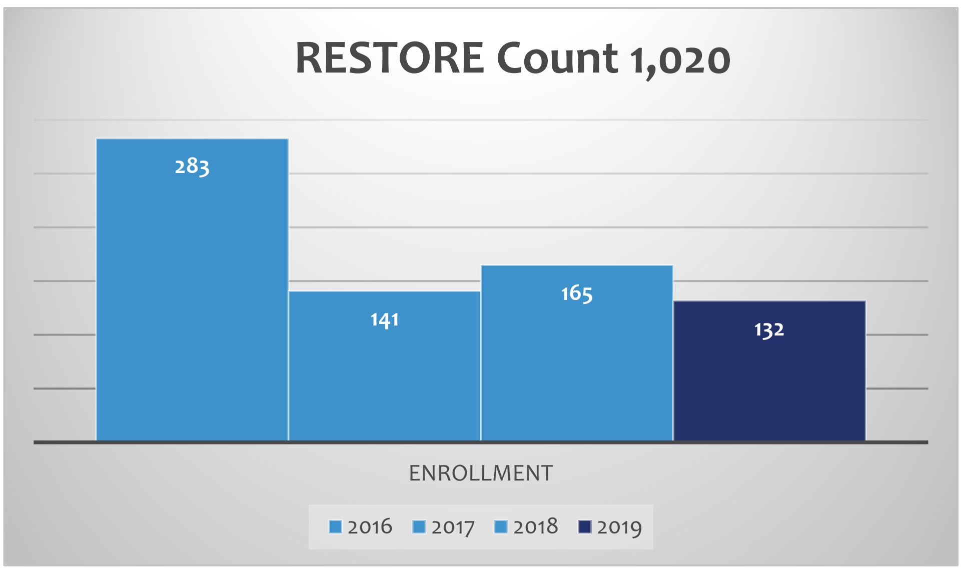
Along with growth in telerehabilitation, a concurrent need has arisen for standardized methods of tele-evaluation.
OBJECTIVE: To examine the feasibility of using the Kinect sensor in an objective, computerized clinical assessment of upper limb motor categories.
DESIGN: We developed a computerized Mallet classification using the Kinect sensor. Accuracy of computer scoring was assessed on the basis of reference scores determined collaboratively by multiple evaluators from reviewing video recording of movements. In addition, using the reference score, we assessed the accuracy of the typical clinical procedure in which scores were determined immediately on the basis of visual observation. The accuracy of the computer scores was compared with that of the typical clinical procedure.
PARTICIPANTS: Seven patients with stroke and 10 healthy adult participants. Healthy participants intentionally achieved predetermined scores.
OUTCOMES AND MEASURES: Accuracy of the computer scores in comparison with accuracy of the typical clinical procedure (immediate visual assessment).
RESULTS: The computerized assessment placed participants' upper limb movements in motor categories as accurately as did typical clinical procedures.
CONCLUSIONS AND RELEVANCE: Computerized clinical assessment using the Kinect sensor promises to facilitate tele-evaluation and complement telehealth applications.
WHAT THIS ARTICLE ADDS: Computerized clinical assessment can enable patients to conduct evaluations remotely in their homes without therapists present.

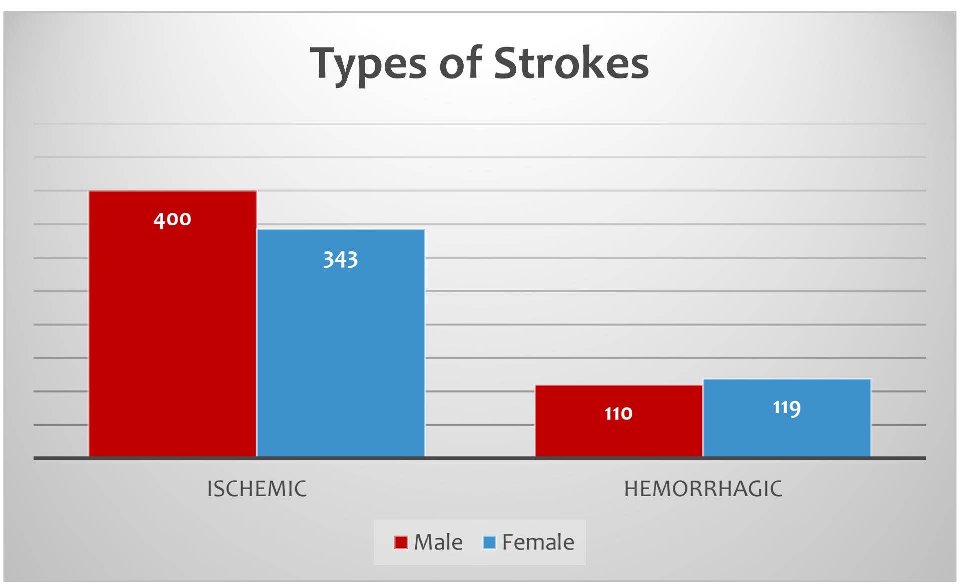
Patient Data in RESTORE

The Stroke Search & Recovery Center has a robust database named RESTORE where all stroke patient's data is consolidated for multi data uses such as recruitment within Stroke studies, data analysis, graduate pilot data, data linkage and custom reporting.

We have enrolled over 1,000+ participants!

RESTORE at a Closer Look





UPCOMING EVENTS

- Stroke Survivor Support Group- January 13th at 6:30pm

National Center for Neuromodulation for Rehabilitation Events

- Advanced Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) Symposium- March 12th & 13th
- Spinal Cord Plasticity in Motor Control Meeting- March 23rd
- Advanced Operant Conditioning of EMG Evoked Potential Workshop- March 24th through 26th

SAVE THE DATE

- Participant Appreciation Day- Sunday March 22nd at The Cooper River Room at Mt. Pleasant Waterfront Park

- Stroke Survivor Support Group:
    - Tuesday Febuary 11th
    - Tuesday March 10th
    - Tuesday April 14th
    - Tuesday May 12th

- 4th Annual Stroke Caregivers Summit- Saturday June 6th at Bon Secours St. Francis Hospital in West Ashley.

More than 859,000 Americans die of heart disease, stroke, or other cardiovascular diseases every year—that's one-third of all US deaths. Leading risk factors for heart disease and stroke are high blood pressure, high low-density lipoprotein (LDL) cholesterol, diabetes, smoking and secondhand smoke exposure, obesity, unhealthy diet, and physical inactivity (CDC 2019).

American Heart Association | American Stroke Association

life is why™

American Heart Association | American Stroke Association
life is why
Together to End Stroke™

High blood pressure equals HIGHER RISK OF STROKE.

NORMAL BLOOD PRESSURE IS BELOW 120/80

STROKE HAPPENS WHEN A CLOT OR RUPTURE INTERRUPTS BLOOD FLOW TO THE BRAIN. WITHOUT OXYGEN-RICH BLOOD, BRAIN CELLS DIE.

Most people who have a first **STROKE** have **HIGH BLOOD PRESSURE.**[1]

80% of strokes can be **PREVENTED.**[2]

Nearly **1 IN 6** American adults with high blood pressure **DON'T KNOW.**[3]

At age 50, people without high blood pressure have a **LIFE EXPECTANCY 5 YEARS LONGER** than people with high blood pressure.[3]

Have your blood pressure checked and keep it in check to **REDUCE** your **RISK OF STROKE.**

1 Neal B et al; Lancet. 2000;356;1955-64 // 2 D'Agostino, R.B. et al. Stroke. 1994;25:40-43 // 3 Mozzafarian D et al. Circulation. 2017;135:e135-139

***Together* To End Stroke™ before it happens. For more information visit Heart.org/HBP**

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STROKE RECOVERY RESEARCH CENTER

A Center of Biomedical Research Excellence (COBRE) in Stroke Recovery at the Medical University of South Carolina