

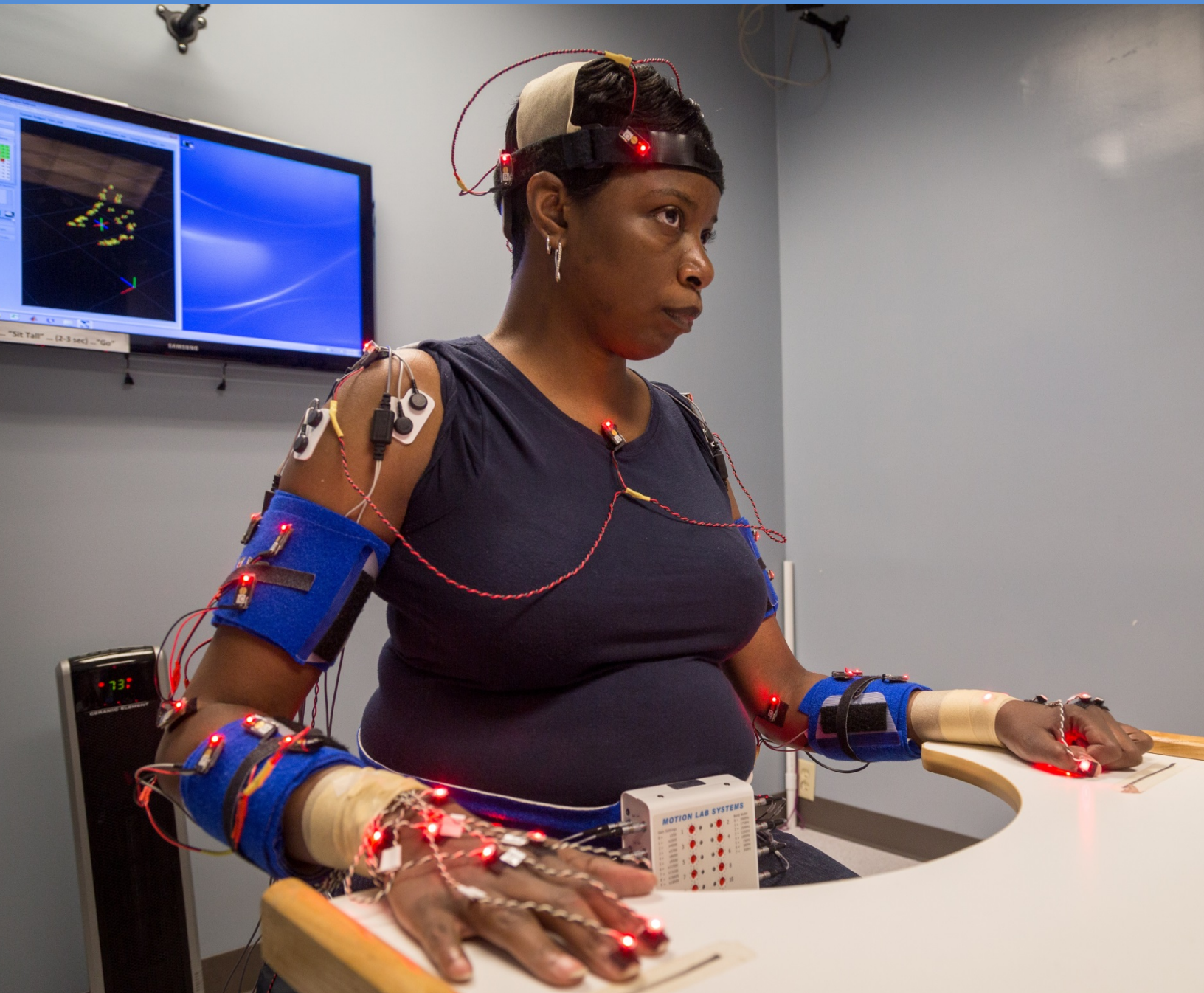
Recovers

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The Newsletter of the Stroke Recovery Research Center | Medical University of South Carolina



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The Medical University of South Carolina has been awarded \$10,823,406 from the National Institutes of Health (NIH) to support an Institutional Development Award (IDeA) Center of Biomedical Research Excellence (P20GM109040). The IDeA program builds research capacities in states that historically have had low levels of NIH funding by supporting basic, clinical and translational research; faculty development; and infrastructure improvements.

From the Director



I am proud to share that we have been very busy the past few months, with much to show for our efforts. Included in our list of accomplishments are the staffing, funding, and development of the Center's four scientific cores, enabling them to offer the services and resources necessary to support the inter-professional group of investigators already at work at the Center. There are currently five active Junior Investigator (JI) grants and five pilot project grants utilizing these COBRE core resources. Additionally, two recent awards signify firsts for the Center. First, an award from Halo Neurosciences is our first industry sponsored clinical trial. This multidisciplinary project uses all of the COBRE cores, highlighting the type of comprehensive research we are championing. Second, being selected as a site in an NIH Telerehab trial will be our first opportunity to participate in a national clinical trial through the StrokeNet.

The excellent feedback offered by our external advisors provided some additional direction for how best to build upon our current momentum as we approach our second year. The first COBRE Annual Meeting was held January 7-8th, hosting the five members of the External Advisory Board (see facing page for EAB membership) who reviewed the Center with a focus on JI projects and core development. Subsequently, they made recommendations regarding unique opportunities for growth and leverage in order to strengthen the overall impact of the Center. Collectively, the board was very impressed by the magnitude of work completed thus far by our talented and collaborative team, and saw great promise in the development of the cores. Included in their recommendations were the explorations of technological interfaces with other state institutions, enhancing research opportunities in the sub-acute phase and telerehabilitation, and strengthening connections with StrokeNet. These recommendations each provide focus and new directions on which the Center can build as it progresses into its second year.

Offering outstanding mentoring opportunities to our JIs remains a critical focus of the Center. Drs. Marom Bikson and Pam Duncan spoke to COBRE investigators in recent months and provided feedback related to the further development of their stroke recovery research. Over the next few months, Dr. Laurel Buxbaum, Dr. Tom Carmichael, Dr. John Wolpaw and Dr. Flavio Frolich will visit MUSC and are scheduled to spend time with the JIs. Significant time spent with these leaders in the field adds valuable experiences to the ongoing scholarly guidance offered through the COBRE's mentoring program.

Much to the benefit of our Center's investigators, the Annual Meeting of the Society for the Neural Control of Movement will be held here in Charleston in April. Not only will the Annual Meeting offer opportunities for Center investigators to gain valuable insight, but the scheduled satellite conference entitled Neural Mechanisms of Rehabilitation will highlight a variety of presentations particularly relevant for stroke recovery research. With key COBRE members involved in the planning of this conference, it represents a direct product of the COBRE and its mission to work across disciplines to become a national resource for stroke recovery researchers.

As our first grant year comes to a close and we start our second one, I am thrilled with our progress and excited for our future.

Steve Kautz, PhD
Director, Stroke Recovery Research Center

The **Stroke Recovery Research Center**
welcomed its **External Advisory Board**
for the first COBRE Annual Meeting January 7-8, 2015

Chairman

Steven L. Wolf, Ph.D., PT, FAPTA, FAHA
Emory University School of Medicine

Steve Cramer, MD
University of California, Irvine, School of Medicine

Argye Beth Hillis, MD, MA
Johns Hopkins University School of Medicine

Felipe Fregni, MD, PhD, MPH, MEd
Harvard Medical School

Randolph J. Nudo, Ph.D.
University of Kansas Medical Center

We thank our advisors for their recommendations and thoughtful consideration!

Guest Scholar



Pamela W. Duncan, PhD, FAPTA, FAHA met with the COBRE Executive Committee and Junior Investigators on January 23, 2015. Dr. Duncan is currently a Professor of Neurology and Senior Policy Advisor for Innovations and Transitional Outcomes at Wake Forest Baptist Medical Center, and is one of the world leaders in stroke rehabilitation. She was in Charleston for the inaugural graduation of the Physical Therapy Neurological Residency Program, at which she presented the keynote address entitled “Redesigning and Transforming Neurologic Physical Therapy for Quality and Value Driven Outcomes: Examples from Stroke Research and Care”. Dr. Duncan is a

longtime collaborator of Dr. Kautz and several of the COBRE investigators, including Dr. Bowden who also serves as the Director of the Neurological Residency. In her current position, Dr. Duncan has transitioned away from rehabilitation clinical trials, and is instead focusing on the long term functional ramifications of acute care and discharge planning. Of particular interests are the prevention of secondary health conditions and reducing the rate of readmission. Over lunch, the COBRE team had the opportunity to discuss with Dr. Duncan each research core and junior investigator project and to provide information regarding multiple aspects of stroke recovery. Dr. Duncan urged the stroke recovery team to increase partnership with the Stroke.Net clinical trial team to incorporate the concept of recovery into acute/sub-acute interventions. Much of the conversation revolved around ways to increase efficiency of clinical translation, and Dr. Duncan highlighted her current efforts at directly impacting post-acute care, which is a source of rapidly spiraling medical cost. In closing, she challenged the team to think outside of the tradition track for research funding and to increase exploration of industry sponsorships and other funding mechanisms to maximize the impact of the stroke recovery outcomes.

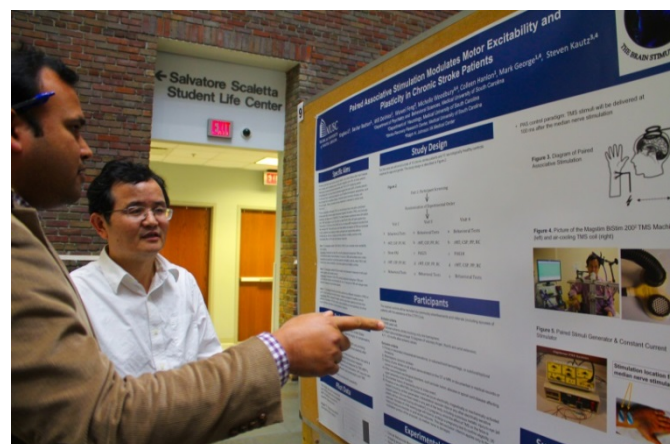
Poster Presentation

A highlight of the COBRE Annual Meeting was the Poster Presentation showcasing the scope of stroke recovery research at MUSC. All university stroke recovery investigators were invited to present, highlighting the underpinnings of research upon which the Stroke Recovery Research Center (SRRC) aims to build. This event exemplified SRRC's commitment to facilitate mentoring opportunities and multidisciplinary collaborations, to advance translational clinical research.

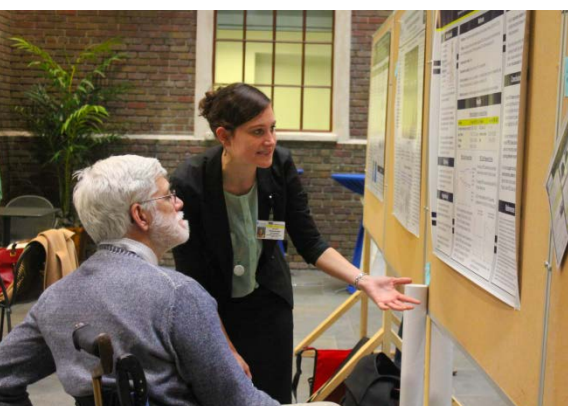
In attendance to review the posters were members the COBRE leadership, faculty members from the Occupational Therapy and Physical Therapy Departments, the COBRE's external advisors, and special guest Dr. Mark Sothmann, Vice President for Academic Affairs and Provost. The occasion provided the 18 presenters representing a wide array of disciplines with valuable feedback to strengthen current projects and inform future studies related to stroke recovery.



Pictured L to R: Charalambos Charalambous, Viswanathan Ramakrishnan and Jihad Obeid



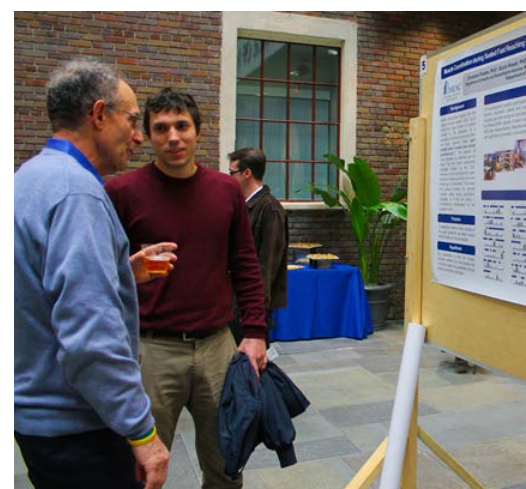
Pictured L to R: Deepak Kumar and Xingbao Li



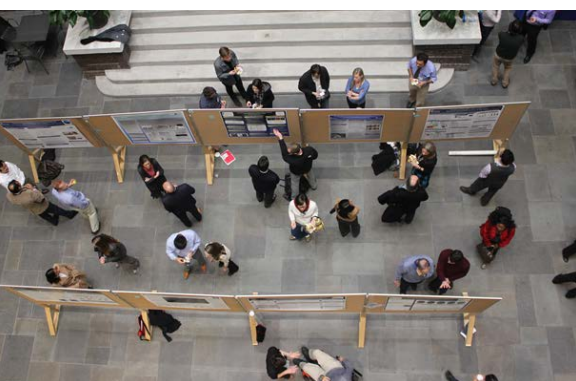
Pictured L to R: Peter Bowman, Janina Wilmskoetter

Poster Presenters:

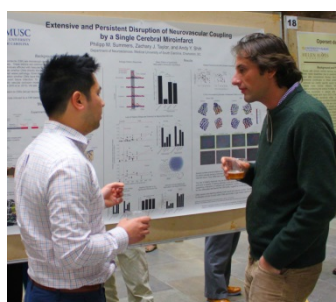
Ezequiel Gleichgerrcht
Jane E. Joseph
Janina Wilmskoetter
Charalambos Charalambous
Christian Finetto
Kelly Anderson
Shraddha Srivastava
Xingbao Li
Alexander Awgulewitsch
Jesse Dean
Donna Roberts
Stephen Tomlinson
Pratik Y. Chhatbar
Rachel Ann Weber
Spencer J. Bell
Andy Shih
Aiko Thompson



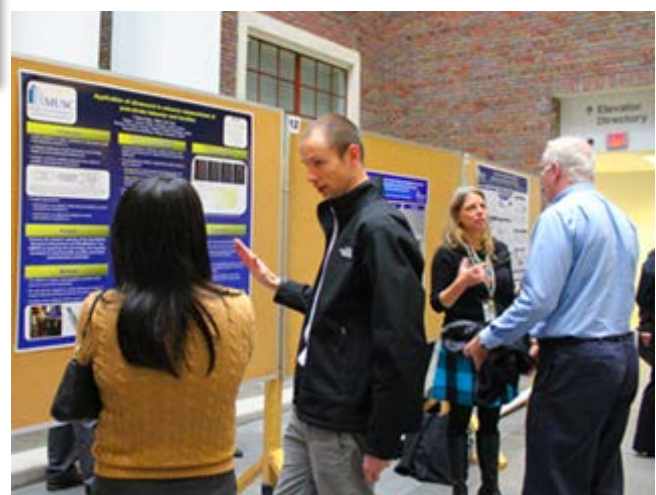
Pictured L to R: Steve Wolf and Christian Finetto



Aerial view of the Stroke Recovery Research Poster Presentation held in the CHP Atrium



Pictured L to R: Andy Shih and Manuel Levy



Pictured L to R: Aiko Thompson, Jesse Dean, Donna Roberts, and Mark Van Horn

Publication Highlight

The following publication represents the type of collaborative project the Stroke Recovery Research Center was created to promote. Featuring investigators working within the NeuroImaging and Brain Stimulation Cores, this highlights the first collaboration for the group of COBRE affiliated investigators working in animal research.

Diffusional Kurtosis and Diffusion Tensor Imaging Reveal Different Time-Sensitive Stroke-Induced Microstructural Changes

Rachel A. Weber, BA; Edward S. Hui, PhD; Jens H. Jensen, PhD; Xingju Nie, PhD; Maria F. Falangola, MD, PhD; Joseph A. Helpert, PhD; DeAnna L. Adkins, PhD

Background and Purpose—Diffusion MRI is a promising, clinically feasible imaging technique commonly used to describe white matter changes after stroke. We investigated the sensitivity of diffusion MRI to detect microstructural alterations in gray matter after sensorimotor cortex stroke in adult male rats.

Methods—The mean diffusivity (MD) and mean kurtosis of perilesional motor cortex were compared with measures in the contralesional forelimb area of sensorimotor cortex at 2 hours, 24 hours, 72 hours, or 25 days after surgery. MD and mean kurtosis were correlated to the surface densities of glia, dendrites, and axons.

Results—Perilesional mean kurtosis was increased at 72 hours and 25 days after stroke, whereas MD was no longer different from contralesional sensorimotor cortex at 24 hours after stroke. There was a significant increase in the density of glial processes at 72 hours after stroke in perilesional motor cortex, which correlated with perilesional MD.

Conclusions—These data support that mean kurtosis and MD provide different but complimentary information on acute and chronic changes in perilesional cortex. Glia infiltration is associated with pseudonormalization of MD in the perilesional motor cortex at 72 hours after lesion; however, this association is absent 25 days after lesion. These data suggest that there are likely several different, time-specific microstructural changes underlying these 2 complimentary diffusion measures.

(Stroke. 2015;46:00-00. DOI: 10.1161/STROKEAHA.114.006782.)

Key Words: diffusion tensor imaging □ glial fibrillary acidic protein □ ischemia □ motor cortex □ stroke

Welcome to the Team!

Cheryl Grant, Recruitment Coordinator



As a new member of the Clinical and Translational Tools and Resources (CTTR) Core, Cheryl Grant will coordinate acute recruitment efforts for the Registry for Stroke Recovery, RESTORE. Her primary responsibility will involve connecting with patients who have been admitted to MUSC following a stroke, as well as following up with them in the outpatient Stroke Clinic in Rutledge Tower. She will provide education on RESTORE, oversee the consent process, and serve as a link between inpatient and outpatient recruitment efforts, informing stroke survivors on the full spectrum of opportunities available in stroke recovery research. This position was created to coordinate acute recruitment efforts, to provide a large pool of well-characterized patients within RESTORE for investigators to query. This population of subjects who have had a stroke will assist participant recruitment and retention efforts, supporting investigator projects aspiring to better understand neural plasticity and its experience-dependent nature.

In addition, Ms. Grant will further develop collaborative relationships between acute and non-acute study coordinators to simplify the screening process for research participants. As the initial gatekeeper, she will work to limit contact and ensure patients do not become overwhelmed by the variety of research opportunities for which they may qualify. Dr. Robert Adams, CTTR Director, “We are very fortunate to have Ms. Cheryl Grant to head up the all-important recruitment effort. Her integration into the operations of the Stroke Recovery Center is key to effective recruitment and crucial to our success” This is a vital role within the CTTR Core, one which aims to serve and benefit all stroke research at MUSC. We welcome you to the team!

Enrolling Soon: The Registry for Stroke Recovery (RESTORE)



The Clinical and Translational Tools and Resources (CTTR) Core has spent the last several months working to create the Registry for Stroke Recovery (RESTORE), and anticipates the first participant enrollments will begin in the next few weeks. By enlisting a diverse group of professionals to develop this formidable research tool, CTTR has made every effort to offer the capabilities necessary for RESTORE to enhance stroke recovery research. Those involved in RESTORE's design include, the Core and Center's leadership, analysts, software engineers and project managers from the bioinformatics team, biostatisticians, and the investigators and study teams poised to benefit the most from this new resource.

As the centerpiece of the CTTR Core, RESTORE will be utilized by investigators for recruiting and retaining participants, and data sharing, as well as to design, conduct, analyze and advance individual research projects. Robert Adams, M.D., SmartState Biomedical endowed chair in stroke, director of the South Carolina Stroke Center for Economic Excellence, director of the South Carolina REACH Stroke Network and REACH MUSC, is the CTTR Core Director and champion of RESTORE as an effective and groundbreaking vehicle for the advancement of stroke research here at MUSC.

The Contribution of the Bioinformatics Team

In 2008, MUSC invested in their research infrastructure through the development of the Biomedical Informatics Center (BMIC). The BMIC team represents a growing number of informatics experts and software engineers offering research support services for the development of research infrastructural systems.

The Biomedical Informatics (BI) provided by members of the BMIC team, play a key role in establishing and maintaining RESTORE. While the research of the SRRRC focuses on stroke recovery, the BI contribution to the CTTR toolbox informs any point in the research spectrum from prevention to acute treatment through rehabilitation and quality of life. This provides a groundbreaking comprehensive approach enhancing MUSC's research capacity and providing links between biomarkers and data resources enhancing the long-term development of stroke research and translational research.

The Role of Biostatistics: Enhancing Stroke Recovery Research

The Biostatistical Support (STAT) offered through the CTTR Core supports the biostatistical needs of the stroke recovery investigators. This role ensures sound experimental design and analysis, the development of novel biostatistical methods and maximal impact and reliability for study results.

To submit a SPARC request for STAT services go to <http://sparc.musc.edu>



- Choose **SCTR** on the left hand side and choose **Biostatistics, Design & Epidemiology**
- From that tab choose the biostatistics support that is needed (**Data analysis, Power analysis, etc.**) and choose **Continue** on the right
- Follow the prompt to complete a new study and fill in the appropriate fields
- In the Impact Areas please choose **Other** and type "Stroke Recovery COBRE."
- Attach any documents that you feel would be relevant to give the biostatistician background knowledge on your study such as journal articles, proposals, data sets, etc.
- Once you submit the request a biostatistician will be in touch within 24 hours

Please contact Abby Lauer @ lauer@musc.edu with questions regarding STAT's role, or how to submit a SPARC request

COBRE Affiliated Grants

Active Grants

Faculty/PI Name	Title	Funding Agency	Project Dates	Funding
Bowden, Mark	Augmentation of Locomotor Adaptation Post-Stroke	VA/RRD	7/1/13-6/30/18	\$907,000
Dean, Jesse	Post-Stroke Contributors to Increased Energetic Cost and Decreased Gait Stability	VA/RRD	October 2012 – September 2016	\$ 639,100
Feng, Wayne/ Woodbury, Michelle	The Halo-MUSC Motor Stroke Rehabilitation Clinical Trial	Halo Neurosciences	Projected 2/1/15-1/30/16	\$286,770
Finetto, Christian	Biomechanical Assessment of the Relationship between Postural Control and Fine Motor Skills in People with Stroke	MUSC Inter-Professional	Projected 1/1/15-12/31/15	\$20,000
Gregory, Chris	Rural Veterans Telerehabilitation Initiative: RVTRI Stroke	Veterans Administration	10/1/14-9/30/15	\$275,050
Gregory, Chris	Functional Electrical Stimulation Assisted Cycling after Stroke	NIH-DE-CTR	9/16/2013-5/31/15	\$86,650
Gregory, Chris	Skeletal Muscle Plasticity as an Indicator of Functional Performance Post-Stroke	VA/RRD`	10/1/13-9/30/17	\$1,100,000
Woodbury, Michelle	Patient-Targeted Upper Extremity	VA/RRD	4/1/13-3/31/17	\$1,100,00
Woodbury, Michelle	Virtual Environment for Stroke Rehabilitation	NIH-DE-CTR	11/30/14-5/30/15	\$86,000

Grant Applications

Faculty/PI Name	Title	Funding Agency	Project Dates	Funding
Dean, Jesse	Development of mechanism-based interventions for post-stroke gait instability	NIH R01	submitted on March 3, 2015	Awaiting review and decision
Dean, Jesse	Influence of Lateral Stabilization on Walking Ability Post-stroke	NIH R21	to be submitted by March 16, 2015	Awaiting review and decision
Feng, Wayne	Developing a New Generation of Transcranial Current Stimulation Device with Safe Application of Higher Currents and Real-Time Monitoring	MUSC SCTR Discovery Pilot	Pre-application submitted: Nov 21, 2014; Full application submitted: Feb 13, 2015	Awaiting review and decision
Feng, Wayne	Modulating the Brain with Bi-hemispheric Transcranial Direct Current Stimulation and Constraint-Induced Movement Therapy to Enhance Post-stroke Motor Recovery	Doris Duke Charitable Foundation	Pre-proposal submitted: Oct 31, 2014; Full proposal submitted: Feb 24, 2015	Awaiting review and decision

Professional Milestones

Dr. Wayne Feng has been named the Director of the MUSC Vascular Neurology Fellowship program beginning July 1, 2015.

Dr. Wayne Feng has been elected a Fellow of the American Heart Association (FAHA). Bearing the highest organizational distinction for cardiovascular and stroke professionals, the AHA recognizes significant scientific accomplishments, volunteer leadership, and service commitments through this esteemed designation. Congratulations Dr. Feng!





April

To learn more about how to help celebrate OCCUPATIONAL THERAPY month this April visit: <http://www.aota.org>

COBRE Funded Grants

Investigator	Title
Awgulewitsch, Alexander	Exploring Potential Roles of Hox Genes in Stroke Recovery
Bowden, Mark	Excitatory and Inhibitory rTMS as Mechanistic Contributors to Walking Recovery
Dean, Jesse	Application of Ultrasound Technology to Enhance the Quantitative Measurement of Post-stroke Behavior and Function
Feng, Wayne	Optimizing Transcranial Direct Current Stimulation Current and Electrode Montage for Stroke Patients
Gregory, Chris	Treating Depression and Enhancing Locomotor Recovery Post-Stroke
Hanlon, Colleen	Investigating the Neurobiologic Basis for Loss of Cortical Laterality in Chronic Stroke Patients
Li, Xingbao	Paired Associative Stimulation Modulates Motor Excitability and Plasticity in Chronic Stroke Patients
Roberts, Donna	fMRI BOLD Signal as a Biomarker for Optimal Dosing of rTMS of Rehabilitation in Chronic Stroke Patients
Shih, Andy	Microvascular Function and Neuroplasticity after Stroke
Tomlinson, Stephen	Complement-dependent Inflammation and Experience-dependent Neural Plasticity after Stroke



Mark Bowden's project presentation during a monthly COBRE Executive Committee/Junior Investigator Meeting



Neural Mechanisms of Rehabilitation Satellite Meeting: Organized by Center Investigators

The presence of the Annual Meeting of the Society for the Neural Control of Movement, held here in Charleston on April 21-24 (<http://ncm-society.org/default.aspx?PageID=1084>), will provide a great opportunity for center investigators. In addition to the novel content scheduled during the Annual Meeting, there will be a satellite conference entitled Neural Mechanisms of Rehabilitation. At the request of Society leadership, center director Steve Kautz led an organizing committee comprised of DeAnna Adkins, Rick Segal and Aiko Thompson. A significant amount of the programming is in stroke recovery, with the rest still being highly relevant. Most center investigators will be attending.

All interested scientists and clinicians are invited to attend the Neural Mechanisms of Rehabilitation meeting on Monday, April 20th at the Francis Marion Hotel. This one-day satellite meeting is sponsored by the MUSC College of Health Professions and will gather specialists in the fields of neurophysiology, neurology, neuroimaging, brain stimulation and rehabilitation to share state of the art research into the neural underpinnings of rehabilitation from nervous system injury and disease. The goal is to appeal to both basic and clinical scientists by emphasizing translational research and showing what the future of rehabilitation might look like. The program is as follows:

08:40 - 10:40 Session 1: Harnessing sensory and motor experience induced plasticity following injury

Scheduled Presenters:

1. Motor learning-induced brain plasticity in Parkinson's disease

Beth Fisher, PhD, PT, University of Southern California

2. Acquisition of a simple motor skill towards improving locomotion after spinal cord injury

Aiko Thompson, PhD, Medical University of South Carolina

3. Harnessing intermittent hypoxia-induced spinal motor plasticity: breathing and walking after spinal injury

Gordon Mitchell, PhD, University of Florida

4. Combining biological, bionic and rehabilitation interventions: finding the Goldilocks zones in rodent models of SCI

Simon Giszter, PhD, Drexel University

11:00 - 13:00 Session 2: Brain stimulation to enhance plasticity and motor recovery

Scheduled Presenters:

1. Adaptive stimulation approaches to enhancing neuroplasticity and behavioral recovery after brain injury

Randy Nudo, PhD, Kansas University

2. Directing neural plasticity to treat stroke and other neurological disorders

Michael Kilgard, PhD, The University of Texas at Dallas

3. Epidural stimulation to enhance motor recovery after stroke

Jeff Kleim, PhD, Arizona State University

4. Induction of behaviorally significant neuroplastic change with non-invasive brain stimulation

Michael Ridding, PhD, University of Adelaide

13:00 - 15:30 Lunch and Satellite Meeting Poster Session, Carolina Ballroom

15:30 - 17:30 Session 3: Personalization of rehabilitation based on an individual's underlying pathophysiology

Scheduled Presenters:

1. The relationship between post brain lesion neural architecture, neurological deficits and rehabilitation

Leo Bonilha, MD, Medical University of South Carolina

2. Promoting motor learning after stroke: The potential role of genetic variation in brain-derived neurotrophic factor

Darcy Reisman, PhD, PT, University of Delaware

3. Neural mechanisms underlying the loss of independent joint control following unilateral brain injury

Jules Dewald, PhD, PT, Northwestern University

4. Matching upper extremity therapies to the likelihood of meaningful change in individuals with stroke

Catherine Lang, PhD, PT, Washington University

17:30 - 18:00 Session 4: Wrap up: Question and Answer Session

Upcoming Events

March 12, 2015
Executive Committee Meeting

March 26, 2015
Visiting Professor, Dr. Laurel
Buxbaum

April 9, 2015
Executive Committee Meeting

April 13, 2015
Frontiers of Neuroscience Meeting

April 14, 2015
Visiting Professor, Dr. Tom
Carmichael

April 17, 2015
Visiting Professor, Dr. John Wolpaw

April 20, 2015
Neural Mechanisms of Rehabilitation
Satellite Meeting

April 21-24, 2015
Neural Control of Movement Meeting

May 14, 2015
Executive Committee Meeting

Brain Puzzler

Unscramble the ten words below by rearranging the order of the letters -- then fill them in the spaces above to find out why it's useful to exercise your brain on games and puzzles!

L A M E N T

S K I D

H E R C A R E S

R A T E

M E G A S

R E N A L

S W O R D

T A R T S

M U T I L A T E S

P H A S E

Everyone knows that _____ brains continue to _____ and grow, but new _____ suggests that even the brains of older adults are not "frozen." They respond well to _____ exercise such as _____ involving _____ like the ones that follow here. It is also useful to _____ your senses and to seek out new experiences. _____ your brain workouts now and get yourself in _____. It works, as will be shown -- or as they say in Latin, "quod _____ demonstrandum"!

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SUDDEN
numbness or
weakness of
face, arm or leg,
especially on one
side of the body



SUDDEN
confusion,
trouble
speaking or
understanding



SUDDEN
trouble
seeing in one
or both eyes



SUDDEN
trouble walking,
dizziness, loss
of balance or
coordination



SUDDEN
severe
headache
with no
known cause

Act FAST and CALL 9-1-1 IMMEDIATELY



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