TMS Study Explores “Brain Plasticity”, Adaptation in Adults with Autism

Lindsay M. Oberman, PhD, Beth Israel Deaconess Medical Center

The Centers for Disease Control and Prevention currently estimates the prevalence of Autism Spectrum Disorders (ASDs) in the United States at 1 in 88 children—more children than are affected by diabetes, AIDS, cancer, cerebral palsy, cystic fibrosis, muscular dystrophy or Down syndrome combined. ASDs are diagnosed clinically, based on the presence of key behavioral symptoms, but the underlying brain mechanisms causing these symptoms are still unknown.

Discovering the brain mechanisms responsible for the behavioral deficits seen in ASD has been the overarching goal of Dr. Lindsay Oberman’s research career. Dr. Oberman began studying autism when she was a graduate student at University of California, San Diego. There she discovered that a system, known as the mirror neuron system, appeared to be dysfunctional in children with ASD.

The mirror neuron system is a network of brain regions whose main function is to respond when one observes another person behaving. It is thought to play a key role in social skills such as imitation, empathy, understanding other’s thoughts, and communication, all of which are impaired in individuals with ASD.

When Dr. Oberman finished her graduate work, she was awarded a postdoctoral fellowship from NIH to continue her work using a novel technique called Transcranial Magnetic Stimulation (TMS). Using TMS, researchers are able to study how the brain functions by experimentally stimulating a specific region of the brain. Dr. Oberman continued her work exploring the brain mechanisms underlying ASD using Transcranial Magnetic Stimulation (TMS) at Beth Israel Deaconess Medical Center with Dr. Alvaro Pascual-Leone. Here she continued her research in collaboration with Dr. Alvaro Pascual-Leone. Here she continued her work exploring the brain mechanisms underlying ASD using a novel technique called Transcranial Magnetic Stimulation (TMS). Using TMS, researchers are able to study how the brain functions by experimentally stimulating a specific region of the brain.

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President Drew Gilpin Faust and Provost Alan Garber invite you to a university-wide symposium addressing the persistent and unacceptable problem of health disparities in the United States and beyond. What does the best research tell us about the causes of disparities and the optimal strategies for eliminating them? What do various disciplines bring to the table in tackling racial/ethnic disparities in health and health care? How can we as a community leverage our resources to advance science in this area and make a difference “on the ground”?

Join in a discussion of these critical issues with the President, Provost, and leading thinkers from across the university.

When: October 11, 2012 from 2:00pm to 5:15pm (reception to follow)
Where: Tsai Auditorium in the Center for Government and International Studies Building (1730 Cambridge St., Cambridge, MA, 02138)

Registration is required: http://ebmi.catalyst.harvard.edu/eventJsf/disparitiesEvent.jsf

SYMPOSIUM: BUILDING QUALITY IMPROVEMENT AND RESEARCH CAPACITY FOR CLINICAL INNOVATIONS IN PRACTICE

The Harvard Catalyst Safety-net Research Infrastructure and the Massachusetts League of Community Health Centers are sponsoring this one-day conference for primary care providers, and administrators working in safety-net health centers.

Upon completion of this conference, participants will:
- Identify and discuss ways to build organizational research infrastructure as it relates to research and quality improvement
- Describe the uses of the Electronic Health Record (EHR) as it relates to translational research and quality improvement
- Demonstrate knowledge and understanding of how to improve EHR data quality
- Be better equipped to collaborate with external research partners
- Describe the ethical challenges around data security and sharing when conducting research and quality improvement

When: October 12, 2012 from 8:30am to 4:30pm
Where: Hoagland-Pincus Conference Center, UMASS Medical Center (222 Maple Avenue, Shrewsbury, MA, 01545)

Registration is required: http://www.massleague.org/Calendar/Event.php?id=442

HARS V A R D  C A T A L Y S T  s p o t l i g h t s

Announcing Two HCCRC Junior Investigator RFAs

HCCRC Resources RFA

The first is a request for Applications for Junior Investigator funding resources and services offered at the five Clinical Research Centers located at BIDMC, MGH, BWH, and MIT. Funds are available for: Above standard nutrition services (ex. DXA, weighed meals, exercise testing); Above standard nursing services (ex. Frequent blood sampling, 1:1 nursing); Psychometric Testing/Analysis; Polysomnography; HCCRC Ultrasound (ex. Cardiac echo; vascular study); Above-standard sample processing services; Research coordinator support; or -80 or -20 freezer storage*. *Please note: services are institution-specific, please contact the Administrative Director where you plan to/are doing your protocol for services pricing. Lab tests are excluded from this RFA, but will be included in a later RFA.

Funds are available for projects which are investigator-initiated and have current IRB approval and HCCRC approval through the HCCRC Protocol Review system. All resources and services use must be rendered between January 1, 2013- June 28, 2013. Applications are due October 26, 2012 with award announcements by December 14, 2012.

HCCRC Laboratory Testing & Genotyping RFA

The second RFA, coming in early November, will offer funds for laboratory tests and genotyping services. Funds will be available for testing of human blood, urine, or saliva samples (testing of tissue samples is not available) and genotyping services (SNPs: NOT sequencing). Applications will be due near the end of November, and will be awarded in January, 2013.

Both RFAs have the same eligibility requirements: applicants must be the PI on the IRB record for the study, but Associate or Full Professors are not eligible. The maximum request, per RFA, per investigator, is $5,000, but investigators are encouraged to apply for both RFAs.

Full applications for the HCCRC Resources RFA are due Friday, October 26, 2012 by 5:00pm
For more information and to download the complete Resources RFA, visit: http://www.brighamandwomens.org/research/CCI/HCCRC_RFA_CRCservices.aspx
Please direct inquiries about the application process to Seanne_Falconer@hms.harvard.edu.
CRC updates

HCCRC @ MGH

Nurse scientists leading more studies

In collaboration with the Munn Center for Nursing Research at MGH, the HCCRC@MGH has been pleased to support an increasing number of clinical research studies led by nurse scientists. These studies cover a wide range of clinical topics including studies of markers for pressure ulcers (V. Capasso, PhD, NP), metabolic and psychosocial changes associated with menopause among women with HIV (S. Looby, PhD, NP), venous thromboembolism prevention (D. Carroll, PhD, RN and P. Restrepo, BSN, RN), catheter-associated urinary tract infections (M. Sullivan, PhD, NP), and patient’s perceptions of their hospital experience (J. Adams, PhD, RN).

Pediatric research expanding

The number of pediatric research projects at the HCCRC@MGH continues to expand with new, high-impact studies in children with autism, seizure disorders, allergies, and type 1 diabetes mellitus. Dr. Wayne Shreffler’s study aims to develop an effective oral immunotherapy for children with peanut allergy, while Dr. Katherine Martien’s hopes to identify biological measures in early childhood that help diagnose autism and monitor therapeutic outcome. Additionally, Dr. Steven Russell is now studying the use of an artificial pancreas in children with type 1 diabetes and Dr. Nicole Sherry has begun a protocol assessing the impact of alpha-1 antitrypsin in preserving beta cell function and slowing progression of type 1 diabetes. These and other ongoing studies continue to energize the pediatric arm of the HCCRC@MGH, which currently includes 32 active protocols.

HCCRC @ BCH

New Behavioral Science Core

The Clinical Research Center at Boston Children’s Hospital is pleased to announce availability of a new Clinical Behavioral Science core, to be housed within the Department of Psychiatry Program in Behavioral Science. This new core will provide consultation and psychometrician services.

To access this research core, go to: www.childrenshospital.org/crc. For questions, please call co-directors Deborah Waber, PhD at 617-355-6523 or Michelle Bosquet Enlow, PhD at 617-919-4680.

Partial funding for this service is provided by Harvard Catalyst.

New BOD POD Resource

In partnership with the GPU (Gastroenterology Procedure Unit), the HCCRC@BCH will soon have the capability of measuring body mass and body volume, with a calculation of body density, percent fat, and percent fat free mass using age and sex-specific equations via a BOD POD. The BOD POD uses air displacement plethysmography and is an easy, safe and quick (approximately 5 minutes total test time) procedure for patients 10 to 250 kg.

For questions, please email: christopher.duggan@childrens.harvard.edu

HCCRC @ BWH

Ultrasound Service Available

Ultrasound Service at HCCRC@BWH offers comprehensive and non-invasive assessments of cardiac and vascular structure and function, utilizing both ultrasound and arterial tonometry. High-quality cardiac ECHO, brachial artery reactivity, carotid IMT, cerebral and renal resistive index, and aortic augmentation index and pulse wave velocity are available to investigators at various HCCRC locations. Ultrasound is provided for an hourly fee which includes scanning and interpretation by experienced technologists. Experienced investigators may also rent the machines for a lower fee if the additional personnel services are not required.

Outpatient Services at BWH

The HCCRC@BWH offers a variety of outpatient services free of charge or at a subsidized price for investigators. Experienced personnel at all sites perform ultrasounds, phlebotomy, ECGs, vitals, blood and specimen processing. Both an RN and an NP are available to perform IV insertions, and infusions, and to conduct medical histories and physicals. Each BWH outpatient site includes a conference room, as well as facilities for research coordinators and study staff to access computers for subject screening, data entry, analyses, preparation, etc.

HCCRC @ MIT

Renovations improve study experience

Equipped with closed-circuit video monitoring equipment and furniture suitable for studies involving children, the HCCRC@MIT’s newly renovated testing rooms have been very busy lately. The rooms are designed for studies involving behavioral testing and testing with children where a parents presence isn’t ideal. The resulting videos or real-time closed-circuit observation allows for co-scoring of assessments and families to watch the study in progress without interfering with testing. The renovations also included a new comfortable waiting area which includes a play area for participant breaks and a place for siblings to play quietly while waiting for testing to conclude.

MIT BU Brain Collaboration

One of the most active studies at the HCCRC@MIT at the moment is the BILD study (Brain Imaging and Language Development) which requires four hours of behavioral testing at HCCRC@MIT, followed by two hours of fMRI scanning at the Martinos Imaging Center at MIT. This project brought together three investigators from two local universities -- John Gabrieli, PhD, and Kenneth Wexler, PhD both from MIT and Helen Tager-Flusberg, PhD from Boston University. Together, MIT and BU are investigating the brain basis of language and reading abilities and deficits in typically developing children and adults, as well as those with autism and SLI (Specific Language Impairment).

Medical Monitoring Devices

PhD candidates David He and Eric Winnokur, supervised by Dr. Charlie Sodini, are currently conducting a pilot to

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the brain and then measuring its response to that stimulation.

In a recent study published in the European Journal of Neuroscience, Oberman and her colleagues used TMS to explore whether abnormalities in the brain’s propensity to respond and adapt to stimulation (also called brain plasticity) may be abnormal in adults with ASD. To do this, they first stimulated the motor region of the brain to obtain a baseline measure of responsiveness of that region. They then applied a special type of TMS called theta burst stimulation (TBS) to the same region, inducing a change in the responsiveness of that part of the brain. Finally, she continued to probe the responsiveness of this region until it returned to baseline levels. This study was supported by the Harvard Catalyst Clinical Research Center at Beth Israel Deaconess Medical Center, with study visits occurring on the CRC unit as well as at the Berenson Allen Center for NonInvasive Brain Stimulation, supported by CRC off unit nursing resources. Though this protocol induced a modulation in responsiveness in both the ASD and healthy control group, the duration of this effect was significantly longer in the ASD group. Specifically, while controls show a modulation of responsiveness for approximately 30-40 minutes following TBS, the effect lasted for over 75 minutes in individuals with ASD. Furthermore, this group difference is so striking that when an independent sample of ASD patients and healthy controls was evaluated, using solely their response to TBS, the test was able to reliably classify the individual into either ASD or control with a very high accuracy.

Dr. Oberman is now extending this work to children with ASD through a collaboration with Dr. Alexander Rotenberg at Boston Children’s Hospital, a project that was initially funded by a Harvard Catalyst KL2 award, and to elderly individuals with ASD and Schizophrenia with Dr. Larry Seidman at Mass Mental Health Center and Dr. Margaret Bauman at MGH’s Lurie Center. She has also collaborated with other Harvard Catalyst researchers, including Dr. Joseph Gonzalez-Heydrich and Dr. Jonathan Picker at Children’s Hospital to explore whether individuals with a related condition, Fragile X Syndrome, also show abnormal brain plasticity. This portion of Dr. Oberman’s work was partially supported by a Harvard Catalyst pilot grant. In addition to her research, Dr. Oberman also teaches in the Psychology Department at Emmanuel College where she hopes to inspire the next generation of neuroscientists with her unrelenting passion for discovering the inner workings of the brain.

**CRC UPDATES: continued from page 3**

evaluate a wearable vital signs monitor, the most recent project of the Microsystems Technology Laboratory (MTL), which has been supported by the HCCRC@MIT. This device is designed to be an affordable, wearable vital signs and cardiac monitor with broad applicability to the home or hospital. This innovative pilot research has generated two recently published papers (IEEE Annual Conference of Engineering in Medicine and Biology Society, 2010, and 2012). The team is currently preparing to pilot the device in the acute care setting.


**HCCRC @ BIDMC**

**Leadership Changes**

We are pleased to announce that Janet Mullington, PhD has been named HCCRC@BIDMC’s CRC Director. Dr. Mullington, a sleep researcher in Neurology, had previously been our center’s Associate Program Director. Alvaro Pascual-Leone, MD PhD, previously the center’s Director, has taken on a larger Harvard Catalyst role as Program Director of the Harvard Catalyst Clinical Research Center Program and is now our Associate Program Director. Also joining our team is Assistant Program Director, Jody Dushay, MD, an Endocrinology researcher whose work focuses on obesity. Please join us in congratulating these individuals on their new roles within the HCCRC@BIDMC and within Harvard Catalyst.

**Online Scheduling for HCCRC Investigators and Teams**

The HCCRC@BIDMC has been actively using a Harvard Catalyst-developed electronic scheduling system since May, 2012. This system was developed as a collaboration between all the Harvard Catalyst HCCRC sites. The tool allows study teams to book study participant visits from their desktops and increases the efficiency of the scheduling process while also allowing the center to record and track data needed for reporting to Harvard Catalyst and the NIH. An enhanced version will be released in mid-September. We are actively training new users and study teams. If you or a member of your study team has not yet been trained in the system and activated as a user, please contact Michelle Beck (mbeck1@bidmc.harvard.edu) to schedule an orientation to the system.