

## **Brain Stimulation and Therapeutic Modulation Division**

Sarah Lisanby, MD, Division Chief

Department of Psychiatry, Columbia University College of Physicians and Surgeons

New York State Psychiatric Institute

Annual Report for July 1, 2007 – June 30, 2008

### **Overview**

The Brain Stimulation and Therapeutic Modulation (BSTM) Division specializes in the use of emerging electromagnetic means of modulating brain function to study brain behavior relationships and to study and treat psychiatric and neurological disorders. The ability to stimulate targeted brain structures noninvasively has opened for the first time the potential to probe the circuitry underlying brain-based disorders and represents a powerful new tool for treating disorders that fail to respond to conventional therapies. The Division's mission is to promote excellence in research and clinical work using brain stimulation. Its vision is to lead psychiatry in the burgeoning field of brain stimulation and to discover new treatments with a superior risk/benefit ratio. The BSTM encompasses research programs (technology development, preclinical, translational, and clinical) and clinical services (inpatient and outpatient) utilizing existing and emerging brain stimulation and neuromodulation interventions at NYSPI and NYPH. These techniques include cranial electrical stimulation (CES), deep brain stimulation (DBS), electroconvulsive therapy (ECT), implanted cortical stimulation (ICS), magnetic seizure therapy (MST), transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS), and vagus nerve stimulation (VNS). These techniques are applied as probes of brain function, as therapeutic interventions, or in conjunction with functional imaging (e.g., simultaneous TMS/fMRI, TMS/PET, TMS/MRS).

The Technology Development Laboratory (led by Dr. Angel Peterchev) enables the design, modeling, construction, and testing of novel devices for brain stimulation that are purpose-built to match the physiology of the human brain. The objective of the Technology Development Lab is to enhance the functionality of brain stimulation devices using novel technological solutions informed by the neurophysiology and neurodynamics of the human brain. New technologies could enable researchers and clinicians to optimize brain stimulation paradigms for basic science and therapeutic applications. In line with these goals, the Lab carries out design and implementation of novel electromagnetic brain stimulation devices, modeling of the electric and magnetic fields induced in the brain during stimulation, as well as basic research studies on the effect of various stimulation parameters on the subjects' physiological response. The BSTM brings together expertise in the neuroanatomical, cognitive and neurophysiological assessment of the impact of stimulation on brain function in preclinical models and in the clinical setting. Close collaborations with the Molecular Imaging and Neuropathology Division (Drs. Arango, Dwork, Underwood) provide the platform for neuroanatomical and neuropathological studies on the impact of brain stimulation on hippocampal plasticity (including neurogenesis, synaptic remodeling, and gene expression). The Cognition Laboratory (Dr. Terrace) provides custom

neurocognitive batteries to assess the impact of brain stimulation on a rich variety of cognitive functions in preclinical models (including anterograde and retrograde amnesia, working memory, spatial memory, serial list learning, ordinal position, numerosity, and meta-cognition). The Preclinical Brain Stimulation Lab, coupled with the physiological expertise of Dr. Charles Schroeder, performs intracerebral recordings of the neurophysiological effects of brain stimulation. Newly opened this year, the Noninvasive Neuromodulation Neuroscience (N3) Lab (led by Dr. Bruce Luber) specializes in applying brain stimulation techniques in cognitive neuroscience and non-treatment studies.

The clinical research facilities include the Brain Behavior Clinic (BBC, led by Dr. Peter Bulow) at NYSPI, the Brain Stimulation Service at NYPH (led by Dr. Sarah H. Lisanby, and offering a new outpatient ECT service as well as clinical treatment with VNS and TMS), 2 human TMS treatment suites at NYSPI, the TMS Unit of the Program for Imaging and Cognitive Sciences (PICS), Stimulation/Imaging facilities (TMS/fMRI, TMS/PET, TMS/MRS), and the ECT suites at NYSPI and NYPH (ECT Service Line Director - Dr. Sarah H. Lisanby; Medical Director - Dr. Joan Prudic). Disorders currently under study include depression (unipolar and bipolar), schizophrenia, anxiety disorders (panic, OCD), autism, movement disorders (Tourette's Syndrome and cerebral palsy), and depersonalization disorder.

## **Staff**

Sarah H. Lisanby, MD, Division Chief, Professor of Clinical Psychiatry  
Bruce Bassie, Graduate Student, Electrical Engineering and Psychiatry  
Fortunato Battaglia, MD, PhD, Visiting Assistant Professor of Psychiatry  
Julien Besle, PhD, Postdoctoral Research Fellow  
Peter Bulow, MD, Assistant Clinical Professor of Psychiatry  
Chi-Ming Chen, PhD, Postdoctoral Research Scientist  
Yael Cycowicz, PhD, Associate Research Scientist  
Zhi De Deng, Graduate Student, Electrical Engineering and Psychiatry  
Linda Fitzsimmons, MS, RNC, ECT Nurse Manager  
Kathleen Friel, PhD, Assistant Professor of Clinical Psychology (in Psychiatry)  
Reza Jalinous, PhD, Adjunct Assistant Professor of Neuroscience (in Psychiatry)  
Alleyama Karyat, RN, Nurse  
Bruce Luber, PhD, Assistant Professor of Clinical Psychology (in Psychiatry)  
Antonio Mantovani, MD, PhD, Associate Research Scientist  
Shawn McClintock, PhD, Postdoctoral Research Fellow  
Janet Mindes, PhD, Education Director  
Angel Peterchev, PhD, Instructor in Clinical Psychiatry  
Joan Prudic, MD, Research Psychiatrist II, Associate Professor of Clinical Psychiatry  
Stefan Rowny, MD, Postdoctoral Clinical Research Fellow  
Charles Schroeder, PhD, Research Scientist 6  
Salomao Segal, MD, Postdoctoral Research Fellow  
Alexandra Sporn, MD, Assistant Professor of Clinical Psychiatry

Arielle Stanford, MD, Assistant Professor of Clinical Psychiatry  
Herbert Terrace, PhD, Professor of Psychology in Psychiatry  
Nancy Turret, MSW, Social Worker

## Current Research

Active research in the BSTM ranges from basic neuroscience studies on brain behavior relationships, to novel intervention development, to clinical trials. Recent work with deep brain stimulation (DBS), electroconvulsive therapy, magnetic seizure therapy, transcranial magnetic stimulation, transcranial direct current stimulation, vagus nerve stimulation, and brain stimulation technology development is summarized below.

**Deep Brain Stimulation (DBS):** This year the Division launched a randomized controlled trial of the antidepressant efficacy of DBS to Brodman's Area 25 as part of a 3 center trial (PI: Lisanby, Sponsor: ANS). This represents the first trial of DBS for a psychiatric indication at CU/NYSPI, and is a collaborative effort with the department of Neurosurgery (Drs. Robert Goodman and Guy McKhann).

**Electroconvulsive Therapy (ECT):** Continuing the NYSPI tradition of excellence in ECT research, Dr. Lisanby serves as co-PI on a multi-institutional collaborative grant submission on post-ECT relapse prevention entitled "Prolonging remission in depressed elderly." This project, which received a priority score of 107, will test the first algorithm-based system for timing maintenance ECT sessions, and will examine neurobiological indices associated with unstable remission in depressed elderly. This project takes optimal advantage of the Columbia-Cornell ECT system, and expertise at Cornell in neuroimaging markers of unstable remission in geriatric depression (Drs. George Alexopoulos and Robert Young). Dr. Joan Prudic, Medical Director of ECT at NYSPI and NYPI, serves as the co-PI of the Columbia clinical site. This year the Division published the novel finding that ultrabrief pulse ECT substantially lowers the cognitive side effects of ECT.

**Magnetic Seizure Therapy (MST):** MST was developed in the Division as a means of reducing the cognitive side effects of ECT through the focality of magnetic fields. The results demonstrate that MST can induce seizures from focal regions of the cortex that have less involvement of deeper brain structures (such as medial temporal cortex) that are implicated in the amnesic side effects of ECT. Parallel studies in a preclinical model (R01 MH60884, PI: Lisanby) and in patients with depression (supported by grants to Dr. Lisanby from NARSAD, Stanley Foundation, and American Federation for Aging Research) are testing its feasibility and safety. Results include the first publications on the safety of MST (and ECT) in a preclinical model, the finding that MST has a better acute safety profile than ECT in patients with depression, neurophysiological evidence that MST-induced seizure are more focal and result in relative sparing of deeper brain structures compared to ECT, and a publication on the anesthetic considerations for MST. We also found that ECT significantly induces the proliferation of new cells and aberrant sprouting of mossy fibers in the dentate gyrus in a preclinical model. These results have implications for the mechanisms of action of

convulsive therapy, and for antidepressant pathways in general. We completed the first trial of the antidepressant efficacy of MST in patients with major depression. We are now engaged in a Stanley supported 2 center trial of MST in the US, and launched an international cooperative trial with sites in Wales and Scotland (supported by the Medical Research Council Brain Sciences II) using a novel MST device design capable of higher output than the original device. The first human to receive 100 Hz MST was treated as part of this international collaboration. The Division published its report (in the British Journal of Psychiatry) on the first eleven cases receiving 100 Hz MST, demonstrating exceptionally fast recovery of orientation after high dose MST. We also reported in Biological Psychiatry superior cognitive outcomes following chronic treatment with high dose MST compared with ECS. The translational cognition studies were presented at the 2007 American College of Neuropsychopharmacology Hot Topics session, by Dr. Lisanby. Dr. Stefan Rowny has joined the Division as a Postdoctoral fellow to develop work with functional neuroimaging to study the neurobiological effects of MST. Dr. Shawn McClintock, a postdoctoral fellow co-mentored by Dr. Lisanby and Dr. Mustafa Husain at UTSW, is developing translational studies on the cognitive effects of MST funded by a NARSAD Young Investigator Award and a K12 grant. Finally, Dr. Yael Cycowicz has applied her expertise in neurophysiology to the study of MST induced seizures, completing and publishing novel findings on how these seizures differ from ECT, and the potential relevance of those differences to clinical outcome.

**Transcranial Magnetic Stimulation (TMS):** The Division's work with subconvulsive levels of TMS encompasses basic studies using TMS in conjunction with functional imaging as a mapping tool, and clinical trials in the treatment of depression and other disorders. Its basic work with TMS includes active studies on working memory, classical conditioning, deception, visual masking, self-awareness, and language processing. One of its basic cognitive neuroscience projects funded by DARPA (co-PIs: Lisanby and Stern) utilizes fMRI and TMS in the study of the effects of sleep deprivation on working memory circuits. This work has isolated brain networks expressed during task performance, affected by sleep deprivation, and differentially affected as a function of cognitive susceptibility to sleep deprivation. The group published results that TMS stereotaxically applied to nodes in these networks facilitates working memory performance in a frequency- and time-dependent fashion, work led by Dr. Bruce Luber. The Division also published its finding that TMS was able to remediate the effects of sleep deprivation on working memory in Cerebral Cortex. In other projects supported by DARPA, the group published the first demonstration of classical conditioned learning using TMS, a novel result important for the interpretation of behavioral and clinical effects seen with TMS. It also completed a study providing the first demonstration that TMS could slow performance on a deception task in a site and latency dependent fashion, a result important to understanding neural circuitry involved in deceptive processes. The Division continues work on an additional DARPA sponsored project to enhance the restorative properties of sleep using TMS-induced slow wave oscillations. Dr. Arielle Stanford received a CTSA pilot award to use fMRI and TMS to delineate and modulate the circuitry involved in volition, a study that lays the foundation for future work on the pathophysiology of avolition in schizophrenia.

Clinical work with TMS includes active trials in depression (Dr. Lisanby, R01 MH069895), schizophrenia (Dr. Arielle Stanford, K23 MH076976, NARSAD), OCD (Drs. Antonio Mantovani, Blair Simpson, and Brian Fallon), depersonalization disorder (Drs. Mantovani and Dr. Simeon of Mount Sinai, Frontier Fund), Tourette's Disorder (Drs. Mantovani and James Leckman, TSA grant and R21 MH082323), co-morbid panic disorder and depression (Dr. Mantovani, NARSAD), autism (Dr. Alexandra Sporn, supported by a K12, Autism Speaks), and cerebral palsy (Dr. Kathleen Friel, K12). The results of the industry-sponsored (Neuronetics, Columbia PI: Lisanby) pivotal multicenter trial of TMS in the treatment of depression were published and led to FDA approval of TMS for the depression indication. We are midway through a similar NIMH sponsored 4-center trial of TMS for depression (R01 MH069895). Add-ons to this trial are examining genetic polymorphisms relevant to treatment response and fMRI and DTI measures of prefrontal cortex function before and after the course of rTMS treatment (led by Dr. Alexandra Sporn, and supported by NARSAD). We also received a NIDA supplement to study the impact of prefrontal rTMS on measures relevant to nicotine craving. We have an active program with TMS in schizophrenia. Dr. Stanford continues work on her NARSAD and NIMH K23 funded studies using rTMS in the study and treatment of the negative symptoms of schizophrenia. This work dovetails with the Dana supported collaborative grant with Drs. Larry Kegeles, Dikoma Shungu, Arielle Stanford, and SH Lisanby, to map abnormal excitatory and inhibitory neurochemical circuitry in schizophrenia with rTMS and MRS. That project should inform the selection of rTMS dosing to alter GABA/glutamate balance in schizophrenia, and will also serve as a probe of GABA/glutamatergic transmission in schizophrenic patients as compared with controls. We are also supported by the Lieber Center to study the role of gamma oscillations and GABA in working memory deficits in schizophrenia, new work led by Dr. Chi-Ming Chen using TMS to study the functional role of oscillations. Finally, the Division is engaged in the first studies employing TMS and tDCS (see below) in the study and treatment of autism spectrum disorders. Led by Dr. Sporn, and supported by her K12 (co-mentors – Drs. Lisanby, Peterson, and Whitaker), Autism Speaks, and a private donor, studies are underway to examine the neural basis of social deficits and repetitive behaviors in this developmental disorder.

**Transcranial direct current stimulation (tDCS):** tDCS is a noninvasive means of altering endogenous firing rates of cortical neurons using polarization with weak direct currents applied to the scalp. Reports suggest tDCS may have antidepressant properties, and may enhance some forms of memory. Research in this area is supported by DARPA (PI: Lisanby) to test the ability of tDCS to affect working memory. Dr. Peter Bulow's NARSAD supported trial on the antidepressant properties of tDCS applied to prefrontal cortex is underway.

**Vagus Nerve Stimulation (VNS):** VNS was approved for the treatment of resistant major depression, but questions remain regarding patient selection and dose-response relationships. We continue work on two multicenter postmarketing trials to address some of these questions (Treatment Resistant Depression Registry and D21 Dose Finding Study, PI: Lisanby). We also received an investigator-initiated contract to study

of the impact of VNS on TMS measures of cortical excitability in patients with treatment resistant depression (PIs: Mantovani and Lisanby).

**Technology Development:** Led by Dr. Peterchev, the Technology Development Laboratory has expanded with the recruitment of Dr. Reza Jalinous, one of the co-inventors of TMS and Technical Director at the Magstim Company, who was appointed Adjunct Associate Professor. Mr. Zhi-De Deng started Ph.D. thesis with Dr. Peterchev on the topic of TMS technology, the first student co-mentored by Engineering and Psychiatry Departments. The Technology Development Laboratory has made significant advances over the past year in several domains: Controllable pulse shape TMS (cTMS): We have continued the development of a novel TMS device with controllable pulse parameters (cTMS), supported by an R21. cTMS could enable research and clinical uses that have not been previously possible due to technological limitations, and could improve tolerability and efficacy in therapeutic applications. Columbia University submitted a patent application on the cTMS technology, and is in active negotiations with a number of device companies regarding licensing agreements.

**Deep brain TMS (dTMS):** We have submitted an invention disclosure for a novel coil design to enable TMS to reach deeper brain targets noninvasively. Columbia has filed a provisional patent on this technology. MST and ECT modeling: We are studying the relationship between the induced cerebral current intensity and the resulting seizure activity in electroconvulsive therapy (ECT) and magnetic seizure therapy (MST). We have demonstrated that, compared to ECT, MST generates weaker currents and ictal expression in central portions of the brain. This could account for the reduced cognitive side effects of MST that has been reported. This study has also suggested that ECT at current pulse amplitudes lower than those conventionally used could have a more targeted therapeutic effect with potentially less side effects. This work was presented at the annual American College of Neuropsychopharmacology meeting in December 2007 and the 3rd International Conference on Transcranial Magnetic and Direct Current Stimulation, Göttingen, Germany in October 2008. TMS – Imaging Integration: Imaging of brain activity during TMS or other forms of brain stimulation is central to understanding and optimizing research and clinical stimulation paradigms. We have made further progress in the installation of state-of-the-art systems that allow functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) to be carried out simultaneously with TMS. TMS-fMRI integration has been supported by a DARPA grant with co-PI Dr. Lisanby, and a new TMS-EEG system was acquired with funding from a New York State Office of Science, Technology and Academic Research (NYSTAR) award to Dr. Lisanby.

**Cognition Laboratory:** Led by Dr. Terrace and supported by R01s MH040462 (Terrace) and MH60884 (Lisanby), the preclinical cognition laboratory continues to innovate new paradigms to probe the impact of brain stimulation on various aspects of cognition. We published in Biological Psychiatry the first study on the impact of a full course of high dose MST on cognition, finding that it had less of an effect than electroconvulsive shock (ECS), and presented these results at the ACNP Hot Topic session. Other major publications from Dr. Terrace's lab focused on the transfer of

metacognitive skills and hint seeking (Psychological Sciences), cognitive imitation (Animal Cognition), and the “generation effect” (Psychological Sciences).

**Physiology:** Dr. Charles Schroeder’s expertise in multichannel electrical recording in awake subjects, multisensory integration, and the functional significance of oscillations in information processing has been a productive addition to the Division. His addition has greatly enhanced the Division’s ongoing studies of the physiological impact of brain stimulation, and has enabled the group to apply for new grant applications to guide brain stimulation dosing strategies to be optimally tuned to ongoing endogenous physiological properties. Dr. Schroeder is a co-investigator on the NYSTAR award that supports the development of EEG-synchronized TMS delivery, and the Division’s Lieber Center projects on the functional role of gamma oscillations in cognition and schizophrenia. Dr. Schroeder’s R01s are on the physiology of visual dysfunction in schizophrenia (MH060358), somato-auditory convergence (MH061989), and the neurophysiological basis of fMRI (MH067560). Dr. Schroeder supervises Dr. Julien Besle, a postdoctoral fellow, to further develop work in these areas.

**Collaborations:** The BSTM serves as a resource for other groups wishing to utilize brain stimulation techniques to investigate other research questions. Collaborating departments across the University include Biomedical Engineering (Dr. Paul Sadjja), Economics (Decision Science - Dr. Elke Weber), Electrical Engineering (Dr. Kenneth Shepard), Neurology (Sergievsky Center – Dr. Yaakov Stern), Neurosurgery (Drs. Robert Goodman, Guy McKhann, Psychology (Drs. Hakwan Lou, Herbert Terrace, Tor Wager), Radiology (Drs. Truman Brown, Joy Hirsch). Collaborating Divisions within Psychiatry include Anxiety Disorders (Drs. Fallon, Simpson), Child Psychiatry (Drs. Peterson, Whitaker), Cognitive Neuroscience (Dr. Bruder) Molecular Imaging and Neuropathology Division (Drs. Arango, Dwork, Parsey, Underwood), Neurobiology and Behavior, Translational Imaging (Dr. Kegeles), and Translational Neuroscience (Dr. Peter Balsam).

## Education and Training

The BSTM provides rotations to undergraduates, medical students, graduate students, residents, and visiting fellows from Columbia and other universities. The Division supports postdoctoral fellowship lines on its DARPA grants. Zhi-De Deng, a Ph.D. student in the Technology Development Lab advised by Dr. Peterchev, is also affiliated with the Department of Electrical Engineering which provides an outstanding opportunity for interdisciplinary and interdepartmental collaboration. Mr. Deng won a TRANSFORM grant from the CTSA to support his research on the development of novel coils for TMS, which could enable an improvement of therapeutic efficacy and blinding in clinical trials. The BSTM Seminar Series and Journal Club continue to flourish. We continue to offer popular CME programs in TMS and ECT, which are provided free of charge to Columbia trainees and faculty. Dr. Schroeder leads the Oscillations Journal Club that serves as a focus for researchers in Psychiatry, Neurology, and Neurosurgery using

translational means to examine the functional role of oscillations in normal and disordered brain function.

## **Clinical Services**

**Brain Behavior Clinic (BBC):** The BBC at NYSPI specializes in the evaluation and treatment of pharmacotherapy resistant disorders, including mood, anxiety, and psychotic disorders. We enroll patients into approved research protocols when appropriate, and provide post-protocol clinical care following study termination.

**Brain Stimulation Service (BSS):** The BSS at NYPH is a unique specialty program offering expert consultations, treatment, and research into innovations in therapeutic brain stimulation. The BSS is uniquely poised to transition new therapeutic devices into clinical application, given the Division's translational research program that ushers novel treatments from device development through pivotal multi-center clinical trials. As novel device-based therapies become FDA-approved, they are added to the spectrum of treatments offered in the BSS. The BSS represents a mutually beneficial bridge between NYPH and NYSPI, enhancing the quality of the clinical care, while increasing patient access to research protocols. The BSS provides management for outpatient ECT, enabling the ECT service to open on outpatient ECT program.

**Electroconvulsive Therapy (ECT):** The ECT services and NYSPI and NYPH provide state of the art clinical care to patients referred for inpatient and outpatient ECT. The services also support approved research studies on novel forms of convulsive therapy.

## **Grant Awards**

### **NARSAD:**

1. 2007 Young Investigator Award (PI: Mantovani; mentor: Lisanby): rTMS in the treatment of panic disorder with comorbid major depression.
2. 2007 Young Investigator Award (PI: Scalia; co-mentors: Lisanby, Arango): The effects of convulsive therapies for depression on the neuronal organization of the hippocampus.
3. 2007 Young Investigator Award (PI: Sporn; mentor: Lisanby): Genetic Predictors of Antidepressant Response to repetitive Transcranial Magnetic Stimulation (rTMS) in Treatment Resistant Depression.
4. 2008 Young Investigator Award (PI: McClintock; co-mentors: Lisanby, Husain): Neuropsychological Associated Effects of Magnetic Seizure Therapy (MST).

### **National Institutes of Health:**

1. NIH Loan Repayment Program (LRP) (PI: Rowny).
2. NIH Loan Repayment Program (LRP) (PI: Stanford).
3. NIH NBIB R21 EB006855-01 (PI: A Peterchev; coPI: Lisanby): Development of A Novel TMS Device with Controllable Pulse Shape (cTMS)
4. NIH NIA K01 AG031912 (PI: Luber; co-Mentors: Lisanby and Stern): Neural basis of cognitive reserve: fMRI/TMS studies of memory and aging.

5. NIH NIDA Administrative Supplement to NIMH R01 MH69895 (PI: Lisanby): to examine nicotine craving following DLPFC TMS in depression.
6. NIH NIMH K23 MH076976 (PI: Stanford; co-mentors: Lisanby and Malaspina). Negative symptoms of schizophrenia: From phenomenology to targeted treatment.
7. NIH NIMH R01 MH60884 (PI: Lisanby): Magnetic Stimulation Therapy: A New Convulsive Treatment
8. NIH NIMH R01 MH69895 (PI: Lisanby): Optimization of TMS for Depression.
9. NIH NIMH R21 MH082323 (PI: Leckman; PI of Columbia/NYSPI site: Lisanby): Transcranial magnetic stimulation for adults with severe Tourette Syndrome
10. NIH NINDS K01 NS062116 (PI: Friel; co-Mentors: Martin, Lisanby, and Gordon) Mechanisms of cerebral palsy recovery induced by balancing motor cortex activity.
11. CTSA Irving Institute for Clinical and Translational Research (PI: Stanford): Neurocircuitry of Negative Symptoms of Schizophrenia: fMRI and TMS studies
12. CTSA K12 Mentored Career Development Program (PI: Friel; co-mentors: Lisanby, Gordon, Martin). Mechanisms of cerebral palsy recovery induced by balancing motor cortex activity.
13. CTSA K12 Mentored Career Development Program (PI: Sporn; co-mentors: Lisanby, Peterson): Neurocircuitry of Autism Spectrum Disorders: fMRI and TMS studies.
14. CTSA KL2 Clinical Research Scholar Program Awards for Multidisciplinary Clinical Scientist Career Development (PI: McClintock; co-mentors: Lisanby, Husain).
15. CTSA TRANSFORM Translational Certificate Program (PI: Zhi Deng; Dissertation Supervisors: Ken Shepard, Angel Peterchev; TRANSFORM Mentor: Lisanby). Field Shaping and Coil Design for Transcranial Magnetic Stimulation (TMS).

**Private Grants:**

1. Advanced Neuromodulation Systems (PI: Lisanby): A Clinical Evaluation for the Management of Patients with Major Depressive Disorder, Single or Recurrent with Deep Brain Stimulation (DBS).
2. Advanced Neuromodulation Systems (PI: Segal). Brodmann Area 25 Deep Brain Stimulation (DBS) Elicits Dopaminergic and Serotonergic responses: Characterization of Biomarkers with Molecular imaging and a novel PET Ligand
3. Alexander Bodini Research Fellowship (PI: Mantovani; Mentor: Lisanby). Transcranial Magnetic Stimulation for severe Tourette Syndrome (TS).
4. Autism Speaks (PI: Sporn): Transcranial magnetic stimulation (TMS) for the evaluation and treatment of repetitive behavior in subjects with autism spectrum disorders.
5. DARPA Research Contract (PI=Lisanby): Deception Disruption.
6. DARPA Research Contract (PI=Lisanby): Lab to Field: TMS/tDCS studies of conditioning brain response to TMS and tDCS memory enhancement.
7. DARPA Research Contract (PI=Lisanby): TMS-Enhanced Power-Nap: A practical system for inducing slow oscillations during sleep.

8. DARPA Research Contract (PIs: Lisanby/Stern): FMRI/TMS Approaches To Enhancing Performance During Sleep Deprivation.
9. Frontier Fund Award (PI: Mantovani): Neural Circuitry of Depersonalization Disorder: A TMS Study
10. Frontier Fund Award (PI: Peterchev): Real-Time Electroencephalographic Feedback Control of Transcranial Magnetic Stimulation
11. Janssen Translational Neuroscience Fellowship (PI: Segal; Co-Mentors: Lisanby, Moore, Parsey). Neurochemical effects of DBS to BA25: Translational studies in baboons and depressed patients
12. Lieber Center Study (Drs. Lisanby, Stanford, Schroeder, and Kegeles): Working Memory Deficits: GABA to Gamma to Function Tourette Syndrome Association (coPIs: Lisanby and Leckman): Transcranial magnetic stimulation for adults with severe Tourette Syndrome.
13. New York State Office of Mental Health (PI: Prudic): Electroconvulsive Therapy in Chronically Psychotic Patients: Towards Evidence Based Treatment
14. New York State Office of Science, Technology and Academic Research Faculty Development Award (PI: Lisanby). Shaping The Future of Therapeutic Neuromodulation
15. Obsessive Compulsive Foundation Research Award (PI: Mantovani). Optimization of Transcranial Magnetic Stimulation in Obsessive-Compulsive Disorder: A Sham Controlled Randomized Clinical Trial of MRI-Guided TMS.
16. Stanley Foundation Research Grant (PI: Lisanby). Magnetic Seizure Therapy (MST) for the Treatment of Depression.

## **Awards and Honors**

1. Dr. Lisanby was selected as a 2008-2009 Fellow of the Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program for Women. This is an intensive one-year program of leadership training with extensive coaching, networking and mentoring opportunities aimed at expanding the national pool of qualified women candidates for leadership in academic medicine, dentistry and public health. Acceptance into ELAM is determined through an annual competitive selection process, in which approximately 48 candidates are chosen each year.
2. Dr. Shawn McClintock was selected for the Summer Research Institute on Randomized Controlled Clinical Trials Sponsored by OBSSR. This is an award for 25 individuals who are selected on a competitive basis to attend a training workshop focused on developing highly trained Academic Investigators.
3. Drs. Stefan Rowny and Shawn McClintock were selected for the Summer Research Institute in Geriatric Psychiatry Sponsored by NIMH. This is an award for 25 individuals who are selected on a competitive basis to attend a training workshop focusing on developing academic investigators in areas involving geriatric psychiatry.
4. Dr. Peter Bulow's sculpture "Alzheimer's Madonna" was featured on the Cover of the American Journal of Psychiatry

5. Dr. Lisanby was appointed as the Chair of the American Psychiatric Association Task Force to Revise the Guidelines on Electroconvulsive Therapy (ECT)
6. Dr. Antonio Mantovani was selected for the Alexander Bodini Research Fellowship Award.
7. Dr. Salomao Segal received the Janssen Translational Neuroscience Fellowship.
8. Dr. Peter Bulow was promoted to Assistant Clinical Professor of Psychiatry.
9. Dr. Antonio Mantovani was promoted to Associate Research Scientist.
10. Dr. Bruce Luber was promoted to Assistant Professor of Clinical Psychology in Psychiatry.
11. Dr. Sarah H. Lisanby was promoted to Professor of Clinical Psychiatry.

## Highlights

1. FDA approved transcranial magnetic stimulation (TMS) for the treatment of depression, based in part on research conducted in the Division, including Lisanby et al. Daily Left Prefrontal Repetitive Transcranial Magnetic Stimulation in the Acute Treatment of Major Depression: Clinical Predictors of Outcome in a Multisite, Randomized Controlled Clinical Trial. *Neuropsychopharmacology*. 2008.
2. New K01 and K12 grants were awarded to Drs. Kathleen Friel (K12 and NINDS K01), Bruce Luber (NIA K01), Shawn McClintock (K12).
3. New Patent filed on novel TMS coil design developed in the Division: Peterchev, Lisanby, Deng (2008). *Methods, Apparatus, and Systems for Magnetic Stimulation*. U.S. Patent Application. Assignee: Columbia University. This is a patent application for coils designed to stimulate deeper brain targets with transcranial magnetic stimulation.
4. Dr. Shawn McClintock received a NARSAD 2008 Young Investigator Award (co-mentors: Lisanby, Husain): *Neuropsychological Associated Effects of Magnetic Seizure Therapy (MST)*
5. Dr. Charles Schroeder and his group published in *Science* their original findings on the functional role of neural oscillations (Lakatos P, Karmos G, Mehta AD, Ulbert I, Schroeder CE. *Entrainment of neuronal oscillations as a mechanism of attentional selection*. *Science*. 2008 Apr 4;320(5872):110-3.)

## New Faculty

This year the Division welcomed two new Division Members (Drs. Friel and Segal). Dr. Friel performs translational studies on cerebral palsy. She received both a K12 and a NIH K01 from NINDS to study the mechanisms of action of motor function recovery in cerebral palsy following constraint therapy. She will employ TMS as a noninvasive probe to examine the mechanisms of motor cortex remapping following constraint therapy. This work is co-mentored by Drs. Lisanby, Andrew Gordon (Teacher's College), and Jack Martin. Dr. Salomao Segal joined the Division to pursue studies on the mechanisms of action of deep brain stimulation. Funded by a Janssen Translational Neuroscience Fellowship (Co-Mentors: Lisanby, Moore, Parsey) and a grant from ANS,

Dr. Segal will study the neurochemical effects of DBS to BA25 in depressed patients using PET. We also congratulate Drs. Bulow and Mantovani on their promotions from fellow to faculty status.

## Publications

Avery, D.H., Isenberg, K.E., Sampson, S.M., Janicak, P.G., Lisanby, S.H., Maixner, D., Loo, C., George, M.S.: Transcranial magnetic stimulation (TMS) in the Acute Treatment of Major Depression: Clinical Response in an Open-Label Extension Trial. *J Clinical Psychiatry*. 2008;69:441-451.

Bajbouj, M., Gallinat, J., Lang, U.E., Hellen, F., Vesper, J., Lisanby, S.H., Danker-Hopfe, H., Neu, P.: Motor cortex excitability after vagus nerve stimulation in major depression. *Journal of Clinical Psychopharmacology*. 2007;27:156-159.

Chen, C.M., Lakatos, P., Shah, A.S., Mehta, A.D., Givre, S.J., Javitt, D.C., & Schroeder, C.E. (2007). Functional anatomy and interaction of fast and slow visual pathways in macaque monkeys. *Cerebral Cortex*, 17, 1561-1569.

Christensen, J.R. Larsen, B.K, Lisanby, SH, Scalia, J, Arango, V, Dwork, AJ, Pakkenberg, B: Neocortical and hippocampal neuron and glial cell numbers of the rhesus monkey. *The Anatomical Record*. 2007, 290:330-40.

Cycowicz YM, Luber B, Spellman T, Lisanby SH. Differential Neurophysiological Effects of Magnetic Seizure Therapy (MST) and Electroconvulsive Shock (ECS) in Non-Human Primates. *Clinical EEG & Neuroscience*. 39:144-149.

Cycowicz YM, Luber B, Spellman T, Lisanby SH. Differential Neurophysiological Effects of High Dose Magnetic Seizure Therapy (HD-MST) and Electroconvulsive Shock (ECS) in Non-Human Primates. *J ECT*. In Press.

Demitrack, M.A., Lisanby, S.H.: Methodological Issues in Clinical Trial Design for TMS: Clinical and Research Implications of This New Therapeutic Platform. Chapter 39 in Lisanby, S. H. (Section Editor), Wassermann, E.M., Epstein, C.M., Ziemann, U., Walsh, V., Paus, T., and Lisanby, S.H. (Volume Editors). *Oxford Handbook of Transcranial Stimulation*. Oxford University Press. 2008. Pp. 621-632.

Deng, Z.D., Peterchev, A., Lisanby, S.H.: Coil design considerations for deep-brain transcranial magnetic stimulation (dTMS). 30th Annual International IEEE EMBS Conference Proceedings. August 24, 2008.

Fallon, B., Lipkin, R.B., Corbera, K.M., Yu, S., Nobler, M.S., Keilp, J., Lisanby, S.H., Moeller, J.R., Slavov, I., Van Heertum, R., Mensh, B.D., Sackeim, H.A.: Regional cerebral blood flow and metabolic rate in persistent Lyme Encephalopathy. *Archives of General Psychiatry*. In Press.

Greenberg, B.D., Lisanby, S.H.: TMS in the Study and Treatment of Anxiety Disorders. Chapter 43 in Lisanby, S. H. (Section Editor), Wassermann, E.M., Epstein, C.M., Ziemann, U., Walsh, V., Paus, T., and Lisanby, S.H. (Volume Editors). Oxford Handbook of Transcranial Stimulation. Oxford University Press. 2008. Pp. 685-696.

Husain, M.M., McClintock, S.M., Rush, A.J., Knapp, R., Fink, M., Rummans, T.A., Classen, C., Petrides, G., Biggs, M.M., Mueller, M., Sampson, S., Bailine, S., Lisanby, S. H., Kellner, G.: The Efficacy of Acute ECT in Atypical Depression. J Clinical Psychiatry. 2008;69:406-4011.

Husain MM, Rush AJ, Trivedi MH, McClintock SM, Wisniewski SR, Davis L, Luther JF, Zisook S, Fava M. (2007). Pain in Depression: STAR\*D Findings. J Psychosomatic Res, 63, 113-122.

Husain MM, Rush AJ, Wisniewski SR, McClintock SM, Fava M, Nierenberg AA, Davis L, Balasubramani GK, Young E, Abala AA, Trivedi MH. Family history of mood disorder and therapeutic outcome: Findings from STAR\*D. J Clin Psychiatry, In Press.

Husain MM, Trevino K, Siddique HW, McClintock SM. (2008). Alzheimer's Disease: current therapy and future prospects. Neuropsychiatric Disease and Treatment, 4(4), 765-777.

Janicak, P., O'Reardon, J., Sampson, S., Husain, M.M., Lisanby, S.H., Rado, Demitrack, M.: Transcranial Magnetic Stimulation (TMS) in the Treatment of Major Depression: A Comprehensive Summary of Safety Experience from Acute Exposure, Extended Exposure and During Reintroduction Treatment. J Clinical Psychiatry. 2008;69:659-667.

Kellner, C. and Lisanby, S.H.: Flexible Dosing Schedules for Continuation ECT. J ECT. 2008: 177-178.

Kirov, G., Ebmeier, K., Scott, A., Atkins, M., Khalid, N., Carrick, L., Stanfield, A., O'Carroll, R.E., Husain, M.M., Lisanby, S.H.: Quick recovery of orientation after Magnetic seizure therapy major depressive disorder. Br J Psychiatry. 2008. 193:152-155.

Kornell N, Terrace HS. The generation effect in monkeys. Psychol Sci. 2007 Aug;18(8):682-5.

Kornell N, Son LK, Terrace HS. Transfer of metacognitive skills and hint seeking in monkeys. Psychol Sci. 2007 Jan;18(1):64-71.

Lakatos P, Karmos G, Mehta AD, Ulbert I, Schroeder CE. Entrainment of neuronal oscillations as a mechanism of attentional selection. Science. 2008 Apr 4;320(5872):110-3.

Lisanby, S.H., Husain, M.M., Rosenquist, P., Maixner, D., Gutierrez, Krystal, A., Gilmer, Marangell, Aaronson, S., Daskalakis, J., Canterbury, Richelson, E., Sackeim, H.A, George, M.S.: Daily left prefrontal repetitive transcranial magnetic stimulation in the acute treatment of Major Depression: Clinical predictors of outcome in a multisite, randomized controlled clinical trial. *Neuropsychopharmacology*. 2008. Aug 13 [Epub ahead of print].

Lisanby, S.H., Peterchev, A.: Magnetic Seizure Therapy for the Treatment of Depression. Pp. 155-171 In Marcolin, M.A. and Padberg, F. (Eds). *Transcranial Brain Stimulation for Treatment of Psychiatric Disorders*. Karger Publishers. *Advances in Biological Psychiatry Series Volume 23*, D. Ebert, K.P. Ebmeier, W.F. Gattaz, W.P. Kaschka (Series Eds). 2007

Lisanby, S.H., Sampson, S., Husain, M.M., Petrides, G., Knapp, R., McCall, V., Young, R., Prudic, J., Kellner, C.H.: Towards Individualized Post-Electroconvulsive Therapy Care: Piloting the Symptom-Titrated Algorithm-Based Longitudinal ECT (STABLE) Intervention. *J ECT*. 2008. 24:179-182.

Lisanby, S.H.: In Reply: Electroconvulsive Therapy for Depression. *NEJM*. 2008, 358:645-646.

Lisanby, S.H.: Electroconvulsive Therapy for Depression. Invited "Clinical Therapeutics" article. *New England Journal of Medicine*. 2007; 357:1939-1945.

Luber, B., Balsam, P., Nguyen, T., Gross, M., and Lisanby, S.H.: Classical Conditioned Learning Using Transcranial Magnetic Stimulation. *Experimental Brain Research. Exp Brain Res*. 2007; 183(3):361-369.

Luber, B., Fisher, C., Appelbaum, P.S., Ploesser, M., Lisanby, S.H. Non-invasive brain stimulation in the detection of deception: Challenge and ethical consequences. *Behavioral Sciences and the Law. Special Issue (Erickson, S., Felthous, A.R., Co-Editors)*. In Press.

Luber, B., Kinnunen, L.H., Rakitin, B.C., Ellsasser, R., Stern, Y., Lisanby, S.H.: Facilitation of performance in a working memory task with rTMS stimulation of the precuneus: frequency- and time-dependent effects. *Brain Res*. 2007 Jan 12;1128(1):120-9.

Luber, B., Peterchev, A., Nguyen, T., Sporn, A. & Lisanby, S.H. Application of TMS in Psychophysiological Studies. Chapter 5 in Cacioppo, J.T., Tassinari, L.G., and Berntson, G.G. (Eds): *Handbook of Psychophysiology*, 2nd Ed. Cambridge University Press. 2007. Pp. 120-138.

Luber, B., Stanford, A.D., Bulow, P., Nguyen, T., Rakitin, B.C., Habeck, C., Stern, Y., Lisanby, S.H.: Remediation of sleep-deprivation induced working memory impairment with fMRI-guided Transcranial Magnetic Stimulation. *Cerebral Cortex*. 2008. 18:2077-2085.

Luber, B., Stanford, A.D., Malaspina, D., Lisanby, S.H.: Revisiting the backward masking deficit in schizophrenia: Individual differences in performance and modeling with TMS. *Biological Psychiatry*. 2007; 62(7):793-9. Epub 2007 Jan 17.

Mantovani A, Lisanby SH, Pieraccini F, Olivelli M, Castrogiovanni P, Rossi S.: Repetitive Transcranial Magnetic Stimulation (rTMS) in the treatment of Panic Disorder (PD) with comorbid major depression. *J Affect Disord*. 2007, 102:277-280.

Mantovani A, Stanford AD, Bulow P, Lisanby SH: Focal Brain Stimulation Approaches to Psychiatric Treatment: Transcranial Magnetic Stimulation (TMS), Magnetic Seizure Therapy (MST), Vagus Nerve Stimulation (VNS), Deep Brain Stimulation (DBS), and Transcranial Direct Current Stimulation (tDCS). Chapter 4 Part II in Tyrer, P. and Silk, K. (Eds). *Cambridge Handbook of Effective Treatments in Psychiatry*. Cambridge University Press. 2008. Pp. 83-97.

Mantovani, A., Leckman, J., Grantz, H., King, R.A., Sporn, A., Lisanby, S.H.: Transcranial Magnetic Stimulation of the supplementary motor area in the treatment of Tourette Syndrome. *Clinical Neurophysiology*. 2007; 118(10):2314-2315.

Mantovani, A., Lisanby, S. H.: Transcranial Magnetic Stimulation in the Treatment of Depression. Chapter 5 in George, M.S., Belmaker, R.H., (Eds). *Transcranial Magnetic Stimulation (TMS) in Clinical Psychiatry*, 2nd Edition. Washington, D.C.: American Psychiatric Press. 2007. Pp. 113-152.

McClintock SM, Cullum CM, Husain MM, Luber B, Lisanby SH. (2008). Rapid recovery of orientation following magnetic seizure therapy. *Journal of the International Neuropsychological Society*, 14(Supplement 1), 141.

McClintock SM, Husain MM, Cullum CM, Luber B, Lisanby SH. (2007). Neurocognitive Associated Effects of Magnetic Seizure Therapy. *The Clinical Neuropsychologist*, 21(3), 399.

McClintock SM, Husain MM, Rush AJ, Knapp RG, Fink M, Rummans TA, Claassen C, Petrides G, Biggs MM, Mueller M, Sampson S, Bailine SH, Lisanby SH, Kellner CH. (2008). "ECT not proven for atypical depression" Dr. McClintock and colleagues reply. *J Clin Psychiatry*, 69(10), 1662-1663.

McClintock SM, Ranginwala N, Husain MM. (2008). Electroconvulsive therapy in schizophrenia. In Mueser, and Jeste (Eds.), *Clinical Handbook of Schizophrenia*. New York: The Guilford Press.

Perera, T.D., Coplan, J.D., Lisanby, S.H., Arif, M., Carpio, C., Lipira, C.M., Spitzer, G., Santarelli, L., Scharf, B., Ruggiero, D., Hen, R., Rosoklija, G.B., Rosenblum, L., Sackeim, H.A., Dwork, A.J.: Antidepressant induced neurogenesis in the hippocampus of adult non-human primates. *J Neuroscience*. 27:4894-4901.

Peterchev, A.V., Jalinous, R., Lisanby, S.H.: A novel transcranial magnetic stimulator inducing near rectangular pulses with controllable pulse width (cTMS). *IEEE Transactions on BioMedical Engineering*. 2008. 55:257-66.

Rajkai, C., Lakatos, P., Chen, C.M., Pincze, Z., Karmos, G., & Schroeder, C.E. (2008). Transient cortical excitation at the onset of visual fixation. *Cerebral Cortex*, 18: 200-209.

Rowny, S., and Lisanby, S.H.: Brain Stimulation. Chapter 109 in Tasman, A., Kay, J., Lieberman, J., First, M.B., and Maj M. (Eds) *Psychiatry Third Edition*. John Wiley & Sons, Ltd. 2008. Pp. 2354-2371.

Sackeim, H.A., Prudic, J., Nobler, M.S., Fitzsimmons, L., Lisanby, S.H., Payne, N., Berman, R.M., Brakemeier, E.-L., Perera, T., Devanand, D.P. Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *Brain Stimulation*. 2008;1:71-83.

Scalia, J., Lisanby, S.H., Dwork, A., Johnson, J., Bernhardt, E.R., Arango, V., McCall, V.: Case Report: Neuropathological examination following 91 ECT treatments in a 92 year old woman with late-onset depression. *J ECT*. 2007; 23(2):96-98.

Schroeder CE, Lakatos P, Kajikawa Y, Partan S, Puce A. Neuronal oscillations and visual amplification of speech. *Trends Cogn Sci*. 2008 Mar;12(3):106-13.

Spellman T, McClintock S, Husain M, Terrace H, Lisanby S: Comparative Effects of High Dose Magnetic Seizure Therapy (MST) and Electroconvulsive Shock (ECS) on Cognitive Function in Rhesus Monkeys. *Biological Psychiatry*. 2008. 63:1163-70.

Sporn, A., Lisanby, S.H.: Double Depression and James Avery: Brain Stimulation and Neuromodulation. Chapter 1 in Barnhill, J.W. Ed. *The Approach to the Psychiatric Patient: Case-Based Essays*. American Psychiatric Association Press, Washington, DC. 2008. Pp. 40-45.

Stanford, A.D., Sharif, Z., Corcoran, C., Urban, N., Malaspina, D., Lisanby, S.H.: rTMS Strategies for the study and treatment of schizophrenia: A review. *IJNP*. 2008. 11:563-576.

Stanford, AD, Sporn A, Krystal AD, Weiner, R., Lisanby, S. H.: ECT and Other Somatic Therapies for Mood Disorders. In Gabbard, G. (Ed). *Treatments of DSM-IV TR Psychiatric Disorders: New Revised Edition*. American Psychiatric Publishing, Inc. 2007.

Vorel, S.R., Lisanby, S. H.: Therapeutic potential of TMS induced plasticity in the prefrontal cortex. Chapter 38 in Lisanby, S. H. (Section Editor), Wassermann, E.M., Epstein, C.M., Ziemann, U., Walsh, V., Paus, T., and Lisanby, S.H. (Volume Editors). *Oxford Handbook of Transcranial Stimulation*. Oxford University Press. 2008. Pp. 611-620.

Wassermann, E.M., Epstein, C.M., Ziemann, U., Walsh, V., Paus, T., and Lisanby, S.H. (Editors). Lisanby, S. H. (Section Editor). *Therapeutic Applications of TMS. Oxford Handbook of Transcranial Stimulation.* Oxford University Press. 2008.

Zemon, V., Tsai, J.C., Al-Aswad, L.A., Chen, C.M., Gordon, J., Greenstein, V., Hu, G., Strugstad, E.C., Dhrami-Gavazi, E., & Jindra, L.F. (2008). Novel electrophysiological instrument for rapid and objective assessment of magnocellular deficits associated with glaucoma. *Documenta Ophthalmologica.* In Press.