Overview

The Division of Experimental Therapeutics focuses on development of new treatment approaches for schizophrenia, depression and other severe mental disorders. This division was formed in 2011 by combining the Divisions of Brain Stimulation with a newly created Conte Center for Schizophrenia Research. The Division interacts closely with the Lieber Clinic to conduct early phase clinical studies of novel therapeutic agents, and with the C.O.P.E. Clinic to perform neurophysiological, neuroimaging treatment studies in the schizophrenia prodrome.

The current Program in Brain Stimulation conducts studies using multiple brain stimulation modalities, including Deep Brain Stimulation (DBS), Transcranial magnetic stimulation (TMS), transcranial Direct Current Stimulation (tDCS), magnetic seizure therapy (MST) and electroconvulsive therapy (ECT) for depression, OCD, schizophrenia, cerebral palsy and other disorders. The Program in Brain Stimulation also maintains a clinical program in TMS and ECT, and conducts highly popular CME programs in ECT and TMS.

The Columbia Conte for Schizophrenia Research conducts neurophysiological and neuroimaging investigations into brain mechanisms underlying schizophrenia and other severe mental disorders. Research activities are divided between Columbia University and Nathan Kline Institute for Psychiatric Research. The Center has been at the forefront of investigating the role of glutamatergic /N-methyl-D-aspartate receptor (NMDAR) dysfunction in the pathophysiology of schizophrenia, depression and other disorders and development of novel NMDAR based treatments.

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Current Research

Research activities are conducted both within the context of 1) an NIMH-funded Conte Center for Schizophrenia Research, 2) an ongoing program in Brain Stimulation and Therapeutic Modulation, and 3) an ongoing program in psychopharmacology for schizophrenia and depressive disorders, conducted in collaboration with the Lieber research clinic.

Conte Center
The Conte Center for Schizophrenia research is investigating brain mechanisms underlying persistent cognitive dysfunction in schizophrenia, with particular focus on early sensory processing abnormalities. Research over the past year has continued to highlighted the importance of early sensory disturbances in the pathophysiology of schizophrenia using both behavioral and neurophysiological measures. For example, deficits in social function in patients with schizophrenia have increasingly been shown to result from failures of basic auditory and visual processing. Similarly, during the course of the illness patients suffer a decline in basic skills, such as the ability to read, based upon progressive sensory impairments. Early identification of these deficits is critical to prevention of the functional decline that is typical in the early course of schizophrenia.

Parallel studies are being conducted using intracranial recordings in patients awaiting epilepsy surgery, under the directorship of Dr. Charles Schroeder. These studies have highlighted the basic mechanisms by which the brain extracts information from our complex sensory environment. For example, the brain has the ability to automatically entrain to the rhythm of speech and to use rhythm to pay attention to only a single person in a noisy environment, such as a cocktail party. Studies from individuals with implanted electrodes have highlighted the brain regions and processes that underlie rhythmic entrainment. Schizophrenia patients show deficits in ability to entrain, suggesting that these mechanisms may be relevant to understanding the basis of social dysfunction in schizophrenia and other disorders.

On a more basic level, deficits in neural function in schizophrenia are related to impaired function of N-methyl-D-aspartate (NMDA) type glutamate receptors. Studies continue to investigate the processes by which NMDAR deficits lead to the specific pattern of deficits observed in schizophrenia, such as failures in the initiation of long-term potentiation in memory systems, or of non-linear gain, and temporal integration within cortical brain networks.

Publications (Selected)


Schroeder CE, Lalor EC. What does polarity inversion of extrastriate activity tell us about striate contributions to the early VEP? A comment on Ales et al. (2010). Kelly SP, Neuroimage. 2012 Apr 5. [Epub ahead of print]


**Brain stimulation**

Research in the Division continues to focus on interrelated brain stimulation, neurophysiological assessment and psychopharmacology for serious mental disorders. In brain stimulation, ongoing research studies are investigating effects of Deep Brain Stimulation (DBS) (PI: Dr. Josh Berman), Transcranial magnetic stimulation (TMS) (PIs: Dr. Joshua Berman, Dr. Antonio Mantovani), Magnetic stimulation therapy (MST) (PI: Dr. Stefan Rowny) and Electroconvulsive therapy (ECT) (PI: Dr. Joan Prudic) in depression. In addition, a newer initiative is focusing on use of transcranial electrical stimulation (tES) methods, including transcranial direct current (tDCS), alternating current (tACS) and random noise (tRNS) stimulation in the treatment of multiple disorders (PI: Dr. Pejman Sehatpour).

**DBS:** Dr. Josh Berman continues to site-PI on a multicenter study of DBS in the treatment of refractory depression.

**TMS:** Dr. Josh Berman has received funding from the Brainsway to participate in a multi-center clinical trial of deep TMS in treatment-resistant bipolar disorder. Dr. Berman was also site PI on a prior study of deep TMS for treatment non-responsive major depressive disorder that led to its successful recent FDA clearance for clinical use. TMS continues to be a growth area, with potential applications to schizophrenia, OCD and pain disorders (among others) in addition to schizophrenia.

Dr. Antonio Mantovani is studying the safety, efficacy, mechanisms of action, and predictor of response for brain stimulation treatments using electromagnetic energy to modulate functional activity of brain circuitry in neuropsychiatric disorders. Early findings are that after 4 weeks of open label rTMS, 5/6 patients showed a >25% improvement on the YBOCS OCD scale. MRS studies demonstrated increased GABA and decreased Glx levels in the pre-SMA.

**MST:** Dr. Stefan Rowny is continuing his NIMH-funded studies of magnetic stimulation therapy (MST) in the treatment of geriatric depression. These studies use an experimental MST device produced by MagVenture corporation. Only 3 of these devices are presently available in the US. MST produces a more focused seizure than more traditional ECT approaches and thus reduced risk of side effects such as memory loss. In addition to depression, other potential targets for MST treatments include OCD and PTSD.

**ECT:** The Columbia Program in Brain Stimulation under the direction of Drs. Joshua Berman (Columbia) and Joan Prudic (NYSPI) continues to be a leader in ECT treatment and research. ECT continues to be one of the most effective treatment approaches for
refractory depression and a routine treatment option within the clinical psychiatry program. Over the past year, Dr. Joan Prudic and Jimmy Choi received a NIMH award (R21 MH096104) to develop cognitive training methods for treatment of memory deficits associated with electroconvulsive therapy.

**tDCS:** Dr. Sehatpour received Irving Institute Clinical Trials office Pilot Award for investigation of use of tDCS in treatment of visual processing deficits in schizophrenia.

**Publications:**


**Psychopharmacology**

The division conducts ongoing research into new treatment development for schizophrenia and related disorders, based on glutamate theories. Over the past year, the Department of Psychiatry at Columbia/NYSPI was awarded a $9M contract from the NIMH to run a network entitled New Experimental Medicine Studies: Fast-Fail Trials in Psychotic Spectrum Disorders (FAST-PS) (overall PI: Dr. Jeffrey Lieberman). Other sites within the network include Yale, NYU/NKI, MPRC, UCLA, and UCD. Dr. Javitt serves as PI for the Columbia site, as well as overall co-PI for the overall project. In addition, the division conducts psychopharmacology research projects in collaboration with the Lieber research clinic (Director: Dr. Joshua Kantrowitz). Ongoing projects include a study of the novel α₇ nicotinic agonist EVP-6124 (EnVivo) for treatment of cognitive deficits, the MOSAIC (Management of Schizophrenia in Clinical Practice) funded by Roche/Genentech, and a study of metabolic effects of Fanapt vs. funded by Novartis (PI: Dr. Jake Ballon).

**Publications:**

5. Javitt DC. Capturing the angel in angel dust: twenty years of translational neuroscience studies of NMDA receptor antagonists in animals and humans Running Head: Translational studies with ketamine Schiz Bull. 2012; in press.


**Education and Training**

The Brain Stimulation program continues to host a highly successful CME course on ECT (course director: Dr. Joan Prudic), conducted under the auspices of NYS OMH. In addition, the program hosts a research rotation for 3rd year medical students. This year, the Brain Stimulation program has initiated several new educational, including a new 2-week rotation for PGY-2 residents during which they learn to perform ECT, receive lectures, and observe magnetic brain stimulation, both rTMS and now MST. This is also the inaugural yr. of the clinical geriatric fellowship with a 5 month block for the geriatric fellows on the NYSPI service.

The division is also heavily involved in post-graduate training of both clinical and basic scientists, including the following:

- **Dr. Gaurav Patel** (resident) has received the American Psychiatric Fellowship award for 2013-14, as well as T32 training position at Columbia and will be joining the Division in July, 2014. Dr. Patel will work jointly with Drs. Schroeder and Javitt on his research program.

- Dr. Elana Zion-Golumbic is working with Dr. Schroeder on brain mechanisms of speech entrainment ("Cocktail party") phenomenon. Dr. Zion-Golumbic is funded from an NIMH individual NRSA and has recently been offered a tenure-track position in the Gonda Brain Sciences Center at Bar Ilan University in Israel.

- Dr. Lucia Melloni (fellow) is working with Dr. Schroeder on active sensing & predictive processing in vision. Dr. Melloni is supported by a grant from the Marie Curie Foundation.

- Dr. Niclas Kilian-Hutten (fellow) is working with Dr. Schroeder on multisensory audiovisual interactions in speech processing. Dr. Kilian-Hutten is supported by a grant from the Rubicon Foundation (Holland).

- Dr. Benjamin Morillon (fellow) is working with Dr. Schroeder on motor influences in auditory processing (auditory active sensing -). Dr. Morillon is supported by a grant from the Fryssen Foundation (France).

- Dr. Saskia Haegens (fellow) is working with Dr. Schroeder on alpha band modulation in active somatosensory processing. Dr. Haegens is supported by a grant from the Rubicon Foundation (Holland).

- Drs. Jordi Costa-Faidella (Marie Curie) and Jose Herrero (HFSP) are pursuing studies of monkey neurophysiology at Nathan Kline Institute.

The Division continues to run a Summer Undergraduate Research Program for students interested in pursuing research careers. Ten students will participate during summer, 2013.
Honors and awards

Dr. Javitt continues to serve as councilor-at-large for the Society for Biological Psychiatry, and as a member of the Liaison committee for the American College of Neuropsychopharmacology. Dr. Javitt is also a standing member of the Institute of Medicine *Neuroforum*, Editor-in-chief for conflict articles at *Schizophrenia Bulletin*, an associate editor of the *American Journal of Psychiatry*, and a member of the editorial board of *Schizophrenia Research*.

Dr. Schroeder is a reviewing editor for *Journal of Neuroscience*.

Top 5 papers this year.


Highlights

The Division continues to a leader in the fields of Brain Stimulation, Psychopharmacology and Neurophysiological Assessment of Schizophrenia and other severe mental disorders.

- In Psychopharmacology, NYSPI/Columbia named overall coordinating center for the multi-site FAST-PS project (PI: Dr. Lieberman). Dr. Javitt was named co-PI for the overall project as well as PI of the Columbia node of this network. Drs. Josh Kantrowitz and Ragy Girgis are co-investigators on this project.

- In Brain Stimulation, Drs. Javitt and Kantrowitz received an investigator-initiated research award from the Stanley Foundation to evaluate effectiveness of transcranial direct current stimulation (tDCS) in the treatment of persistent auditory hallucinations in schizophrenia.
• Also in brain stimulation, Dr. Berman received an award from the Brainsway Corporation to evaluate effects of deep brain stimulation on treatment-resistant bipolar disorder.

• Dr. Javitt will receive the 2013 Research Award from the American Psychiatric Association for recognition of his work as part of the TURNS consortium. Co-winners include Drs. Steve Marder (UCLA), Don Goff (NYU) and Bob Buchanan (MPRC). Dr. Javitt will be honored at the APA annual meeting in June, 2013.

• Dr. Gaurav Patel is recipient of the 2013 American Psychiatric Fellowship award from the American Psychiatric Association. Dr. Patel will be honored at the APA annual meeting in June, 2013.

• Drs. Schroeder and Zion-Golumbic published a well-received paper in the journal *Neuron* on neural underpinnings of the Cocktail party phenomenon. The story was picked up by the lay media, including NPR. Further details at [http://www.npr.org/blogs/health/2013/03/07/173613681/hear-that-in-a-din-of-voices-our-brains-can-tune-to-one](http://www.npr.org/blogs/health/2013/03/07/173613681/hear-that-in-a-din-of-voices-our-brains-can-tune-to-one)

• Dr. Pejman Sehatpour received a Clinical Trials Pilot Award from the Irving Institute.