Brain Imaging Center presents:
1st Annual BIC Symposium - 2014
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The Brain Imaging Center at Icahn School of Medicine at Mount Sinai

Davis Auditorium (2nd floor)
Hess Center for Science and Medicine

October 28th, 2014

REGISTRATION & POSTER SETUP
8:15am – 9:00am  2nd floor & Seminar Room B
Free registration: https://mlmsm.edu/bioday/

OPENING REMARKS
9:00 am – 9:15 am  Rita Z. Goldstein, PhD (Chief, Brain Imaging Center, ISMMS)
9:15 am – 9:30 am  Dennis Charney, MD (Dean, ISMMS)
9:30 am – 9:45 am  Eric Nestler, MD (Director, Friedman Brain Institute, ISMMS)

KEYNOTE ADDRESS
9:45 am – 10:45 am  Gregory Farber, PhD (Director, Office of Technology Development and Coordination, NIH)
“The NIH BRAIN Initiative: Current Status, Future Plans, Application to Brain Imaging”

10:45 am – 11:00 am  Coffee Break

SESSION I – TOOLS, Moderator: Zahi Fayad, PhD
11:00 am – 11:15 am  Jungian Xu, PhD “Sinai BIC common imaging protocol”
11:15 am – 11:30 am  Rafael O'Halloran, PhD “Freeze that patient! Motion in (d)MRI and what we are doing about it.”
11:30 am – 11:45 am  Pranit Kundry, PhD “Studying resting state connectivity using multi-echo MRI”
11:45 am – 12:00 pm  Priti Balachandani, PhD “Exploring new ways to visualize the brain through 7T MRI”

SESSION II – Neuroimaging in Cognitive and Emotional Neuroscience, Moderator: Nelly Alia-Klein, PhD
12:00 pm – 12:15 pm  Jin Fan, PhD “Embodied mind: Physiological signals in functional MRI”
12:15 pm – 12:30 pm  Scott Moeller, PhD “Neural correlates of drug choice in human addiction”
12:30 pm – 12:45 pm  Paula Croxson, PhD “Non-human primate imaging”
12:45 pm – 1:00 pm  Michael Michaelides, PhD “DREAMM: A novel biobehavioral in vivo imaging strategy for deciphering cell type-specific whole brain functional anatomy”

1:00 pm – 3:00 pm  Lunch & poster session

SESSION III – Neuroimaging in CNS Disorders, Moderator: Fred Lublin, MD
3:00 pm – 3:15 pm  Matilde Inglese, MD, PhD “Dissecting multiple sclerosis heterogeneity: Insights from molecular and metabolic imaging”
3:15 pm – 3:30 pm  Lazar Fleischer, PhD “Intracellular sodium quantification in the human brain using MRI”
3:30 pm – 3:45 pm  Mary Sano, PhD “Imaging in dementia diagnosis and clinical research”
3:45 pm – 4:00 pm  Sophia Frangou, MD, PhD “A systems neuroscience perspective of schizophrenia and bipolar disorder”

4:00 pm – 4:30 pm  Coffee Break

SESSION IV – Neuroimaging in CNS Disorders, Moderator: Sophia Frangou, MD, PhD
4:30 pm – 4:45 pm  Jeffrey Newcorn, MD “Using fMRI to understand therapeutic mechanisms of ADHD medications”
4:45 pm – 5:00 pm  Jaimie Murrough, MD “Defining neuroimaging biomarkers of depression and rapid antidepressant treatment response”
5:00 pm – 5:15 pm  Harold Koeningberg, MD “Mechanisms of dysregulated emotion and re-establishing emotional control in borderline personality disorder”
5:15 pm – 5:30 pm  Vilma Gabbay, MD “Neuroimmunology of reward processing and anhedonia in adolescents”

CLOSING REMARKS
5:30 pm – 5:40 pm  Rita Z. Goldstein, PhD (Chief, Brain Imaging Center)
5:40 pm – 7:00 pm  Poster session (cont.) & reception: wine and cheese
Dr. Goldstein is a Professor of Psychiatry with a secondary appointment in the Department of Neuroscience at the Icahn School of Medicine at Mount Sinai (ISMMS) in NY. Dr. Goldstein is chief of the Brain Imaging Core (BIC) at ISMMS; she also directs the NARC (Neuropsychoimaging of Addiction and Related Conditions) research group that uses multimodality functional neuroimaging methods to explore the neurobiological basis of impaired cognitive and emotional functioning in human drug addiction and other disorders of self-control. An important application of this research is to facilitate the development of intervention modalities that would improve treatment outcome in drug addiction and other chronically relapsing disorders of self-regulation.

Nationally and internationally known for her neuroimaging and neuropsychological studies in drug addiction, Dr. Goldstein formulated a theoretical model known as Impaired Response Inhibition and Salience Attribution (iRISA). The model uses multiple neuroimaging modalities—including MRI, EEG/ERP, PET and neuropsychological tests—to explore the neurobiological underpinnings of iRISA in drug addiction and related conditions. Her work has contributed to the development of relevant machine-learning algorithms for innovative analyses applied to this multidimensional data set.

Dr. Goldstein’s interests also include pharmacological fMRI, neurofeedback using Brain Computer Interface, and brain stimulation. She has also been exploring the contribution of individual differences, including polymorphisms in monoaminergic genes, to addiction and aggression, with a focus on the neural mechanisms underlying reinforcement learning, risk-taking and extinction, choice and decision-making, and self-awareness and insight into severity of illness.

Dr. Goldstein received her B.A. degree (double major in Psychology and French), cum laude, from Tel Aviv University, Israel, in 1992. She received her Ph.D. degree in Health Clinical Psychology, with award of academic merit, from the University of Miami, FL, in 1999, after completing a yearlong internship in clinical neuropsychology at the Long Island Jewish Medical Center, NY. She then completed her post-doctorate training on a fellowship on Brain Imaging
and Alcohol Abuse from the National Institutes of Health, under the mentorship of Nora D. Volkow (director of NIDA). Dr. Goldstein received her license in clinical psychology in 2002. Dr. Goldstein became Assistant Scientist at the medical research department at Brookhaven National Laboratory in 2002, advancing to the Associate position in 2004, and to a Scientist position in 2006; tenure was awarded in 2008. Dr. Goldstein moved to the Icahn School of Medicine in January 2013. Dr. Goldstein is also an affiliate in the departments of psychology and biomedical engineering at State University of New York at Stony Brook. She has authored or co-authored numerous well-cited peer-reviewed manuscripts and book chapters, focusing on the role of the prefrontal cortex in addiction. She became member of the American College of Neuropsychopharmacology (ACNP) in January 2010, receiving the prestigious Joel Elkes Research Award in 2012 and the Jacob P. Waletzky Award in 2013. Goldstein’s research has been independently funded by several federal and private agencies (including NIDA, NIMH, and NARSAD).

As BIC chief Dr. Goldstein is striving to facilitate optimized research use of ISMMS’s state-of-the-art brain imaging facilities at the Translational and Molecular Imaging Institute (TMII). Adopting a translational (3T, 7T, PET/MR; human and non-human imaging), developmental and cross-generational familial approach, BIC has been developing a standardized processing pipelines to acquire, analyze and manage a comprehensive set of brain scans across a myriad of neuropsychiatric disorders with the goal of accelerating the development of large-scale gene-brain-behavior datasets essential for revolutionizing our understanding of the brain.
Dennis S. Charney, MD, is Anne and Joel Ehrenkranz Dean of the Icahn School of Medicine at Mount Sinai and President for Academic Affairs for the Mount Sinai Health System. He is also a world expert in the neurobiology and treatment of mood and anxiety disorders, making fundamental contributions to the understanding of the causes of human anxiety, fear and depression and the discovery of new treatment for mood and anxiety disorders.

Since Dr. Charney was named Dean in 2004, the Icahn School of Medicine has risen to, and has maintained, its strength among the top 20 institutions in National Institutes of Health (NIH) funding, and it currently ranks fifth in funding per faculty member from the NIH and other sources. With a long track record of strategic recruitments across the biomedical sciences and in genomics, computational biology, entrepreneurship, and information technology, Mount Sinai has cultivated a supercharged, Silicon Valley-like atmosphere in the academic setting. The Icahn School of Medicine is also consistently listed among the top 20 medical schools in the country according to U.S. News & World Report, and in 2009, it received the Spencer Foreman Award for Outstanding Community Service from the Association of American Medical Colleges.

As the sole medical school affiliation for seven hospital campuses in the new Mount Sinai Health System, the Icahn School of Medicine has one of the most expansive training and research footprints in the nation. Early in his tenure as Dean, Dr. Charney unveiled Mount Sinai’s $2.25 billion strategic plan that laid the foundation for the 14 robust Research Institutes that Mount Sinai is known for today. These institutes are hubs of scientific and clinical enterprise, working together to challenge the limits of science and medicine. Within—and across—them, scientists and physicians, who themselves are members of the teaching faculty, can facilitate the development of effective treatments for the most serious medical conditions.

In the Health System, Dr. Charney is currently developing the structure for complementary Clinical Institutes that will serve as Centers of Excellence for cancer, heart disease, diabetes, HIV, pulmonary diseases, and more, with the anticipation that this architecture—compatible research and clinical institutes—will further eliminate silos and generate game-changing models.
in clinical excellence and standards of care. To further advance this goal, Dr. Charney also led the development of a nationally unique partnership between Mount Sinai and Rensselaer Polytechnic Institute in Troy, New York, that is designed to pool Mount Sinai’s expertise in biomedical research and patient care with Rensselaer’s talent in engineering, computation, and prototyping. Together, the institutions are developing the educational programs, research projects, and infrastructure needed to invent novel biomedical technologies while training a new breed of translationally focused scientists.

Dr. Charney’s career began in 1981 at Yale, where, within nine years, he rose from Assistant Professor to Professor of Psychiatry, a position he held from 1990 to 2000. While there, he chaired the NIMH Board of Scientific Counselors, which advises the institute’s director on intramural research programs. In 2000, NIMH recruited Dr. Charney to lead the Mood and Anxiety Disorder Research Program — one of the largest programs of its kind in the world — and the Experimental Therapeutics and Pathophysiology Branch. That year he was also elected to the Institute of Medicine of the National Academy of Sciences. His scientific research has been honored by every major award in his field, and his work in depression has led to new hypotheses regarding the mechanisms of antidepressant drugs and discovery of new and novel therapies for treatment resistant depression including Lithium and Ketamine. The work demonstrating that Ketamine is a rapidly acting antidepressant has been hailed as one of the most exciting developments in antidepressant therapy in more than half a century. More recently, his pioneering research has expanded to include the psychobiological mechanisms of human resilience to stress.

Dr. Charney’s studies on human resilience have culminated in the identification of ten key resilience factors for building the strength to weather and bounce back from stress and trauma. This work is summarized in an inspiring book, Resilience: The Science of Mastering Life’s Greatest Challenges, co-authored by Steven Southwick and published by Cambridge University Press in 2012.

In 2004, Icahn School of Medicine at Mount Sinai recruited Dr. Charney as Dean of Research. In 2007, he became the Dean of the School and Executive Vice President for Academic Affairs of the Medical Center. In 2013, he was named President for Academic Affairs for the Health System.

A prolific author, Dr. Charney has written more than 700 publications, including groundbreaking scientific papers, chapters, and books. He has authored many books, including Neurobiology of Mental Illness (Oxford University Press, USA, Fourth Edition, 2013); The Peace of Mind Prescription: An Authoritative Guide to Finding the Most Effective Treatment for Anxiety and Depression (Houghton Mifflin Harcourt, 2004); The Physicians Guide to Depression and Bipolar Disorders (McGraw-Hill Professional, 2006), Resilience and Mental Health: Challenges Across the Lifespan (Cambridge University Press, 2011), and, as mentioned, Resilience: The Science of Mastering Life’s Greatest Challenges, for lay audiences (Cambridge University Press, 2012).
Eric J. Nestler, MD, PhD  
Nash Family Professor and Chairman,  
Department of Neuroscience  
Director, Friedman Brain Institute  
Icahn School of Medicine at Mount Sinai

Dr. Nestler is the Nash Family Professor of Neuroscience, Chairman of the Department of Neuroscience, and Director of the Brain Institute at the Icahn School of Medicine at Mount Sinai in New York. He received his B.A., Ph.D., and M.D. degrees from Yale University, and completed his residency training in psychiatry at McLean Hospital and Yale in 1987. He then served on the Yale faculty from 1987-2000 where he was the Director of the Division of Molecular Psychiatry, and was Chairman of the Department of Psychiatry at The University of Texas Southwestern Medical Center at Dallas from 2000 to 2008, before moving to Mount Sinai.

Dr. Nestler has served on the Board of Scientific Counselors of the National Institute on Drug Abuse, on the National Advisory Mental Health Council for the National Institute of Mental Health, the National Advisory Drug Abuse Council for the National Institute on Drug Abuse, and as Council member of the American College of Neuropsychopharmacology (President in 2011) and of the Society for Neuroscience. He is also a past member of the Board of Directors of the McKnight Endowment Fund in Neuroscience. Dr. Nestler currently serves as a member of the Scientific Advisory Boards of the National Alliance for Research in Schizophrenia and Depression, the International Mental Health Research Organization, and the Tau Consortium. Dr. Nestler was elected to the Institute of Medicine in 1998 and to the American Academy of Arts and Sciences in 2005.

The goal of Dr. Nestler’s research is to better understand the molecular mechanisms of addiction and depression. His research uses animal models of these disorders to identify the ways in which drugs of abuse or stress change the brain to lead to addiction- or depression-like syndromes, and to use this information to develop improved treatments of these disorders.
Dr. Farber has a B.S. from Penn State University in chemistry (1984) and a Ph.D. from MIT in physical chemistry (1988). Dr. Farber’s research in graduate school involved determining the three dimensional structure and mechanism of the enzyme xylose isomerase in the laboratory of Dr. Gregory A. Petsko. After graduate school, Dr. Farber received a Life Sciences Research Fellowship to work on mechanistic enzymology with Dr. W. W. Cleland at the University of Wisconsin. Following his postdoctoral fellowship, Dr. Farber returned to Penn State as an Assistant Professor of Biochemistry and rose to the rank of Associate Professor with tenure by 1998. His research included work on structural movies of enzyme action, molecular evolution, and mechanistic enzymology.

Following a sabbatical year in the Division of Biological Infrastructure at the National Science Foundation, Dr. Farber decided to stay in government service. He moved to the National Center for Research Resources (NCRR), part of NIH, in 2000. At NCRR, he managed a number centers and individual investigator awards in technology development and bioinformatics, as well as a cohort of interdisciplinary research centers.

In 2009, Dr. Farber became the Director of the Office of Extramural Activities at NCRR. The Office of Extramural Activities oversees the Office of Grants Management and the Office of Review. Dr. Farber also served as the Director of the Office of Construction Grants. That Office managed $1B in construction awards made using American Recovery and Reinvestment Act funds.

In June 2011, Dr. Farber became the Director of the Office of Technology Development and Coordination at the National Institute of Mental Health (NIMH). That office is responsible for coordinating all technology development and bioinformatics activities at NIMH, overseeing the National Database for Autism Research and other NIMH data repositories, managing the NIMH Common Data Element effort, managing the Human Connectome project, managing the BRAIN
Initiative for NIMH, and also overseeing the NIMH Small Business program. Many of these activities, especially NDAR, the Human Connectome project, the BRAIN Initiative, and the technology development portfolio have significant imaging components.

KEYNOTE ADDRESS

The NIH BRAIN Initiative: Current Status, Future Plans, Application to Brain Imaging

The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is a multi-agency project aimed at revolutionizing our understanding of the human brain. The NIH version of the BRAIN Initiative began in April, 2013. Six program announcements were released in December 2013, and the awardees from those program announcements have just been announced. This talk will discuss and review the timeline for the program and will highlight some of the recently announced awards. Plans for NIH BRAIN Initiative activities in FY15 will also be discussed.
Dr. Fayad serves as professor of Radiology and Medicine (Cardiology) at the Mount Sinai School of Medicine. He is the Director of the Translational and Molecular Imaging Institute; Vice chair for Research, Department of Radiology at the Icahn School of Medicine at Mount Sinai. Dr. Fayad’s interdisciplinary and discipline bridging research - from engineering to biology and from pre-clinical to clinical investigations - has been dedicated to the detection and prevention of cardiovascular disease with many seminal contributions in the field of multimodality biomedical imaging (MR, CT, PET and PET/MR) and nanomedicine. He has authored more than 300 peer-reviewed publications (h-index of 64 accessed 07/31/2014 on Thomson Reuters Web of Science), 50 book chapters, and over 400 meeting presentations. He is currently the Principal Investigator of four federal grants/contracts funded by the National Institutes of Health’s National Heart, Lung and Blood Institute and National institute of Biomedical Imaging and Bioengineering with a recent large award from NHLBI to support the Program of Excellence in Nanotechnology. In addition, he serves as Principal Investigator of the Imaging Core of the Mount Sinai National Institute of Health (NIH)/Clinical and Translational Science Awards (CTSA). He is a PI on a project part of the Strategically Focused Prevention Research Network Center grant project funded by the American Heart Association (AHA) to promote cardiovascular health among high-risk New York City children, and their parents, living in Harlem and the Bronx.

He is Associate Editor for the Journal of the American College of Cardiology Imaging (JACC Imaging), Section Editor for Journal of the American College of Cardiology (JACC) and Consulting Editor for Arteriosclerosis Thrombosis and Vascular Biology (ATVB) and past associate Editor of Magnetic Resonance in Medicine (MRM). In 2013, he became a Charter Member, NIH Center of Scientific Review, Clinical Molecular Imaging and Probe Development Study Section.

Dr. Fayad had his engineering trainings at Bradley University (BS, Electrical Engineering ’89) the Johns Hopkins University (MS, Biomedical Engineering ’91) and at the University of Pennsylvania (PhD. Bioengineering ’96). From 1996 to 1997 he was junior faculty in the
Dr. Fayad is the recipient of multiple prestigious awards. In 2007 he was given the John Paul II Medal from Krakow, Poland in recognition for the potential of his work on humankind. As a teacher and mentor, Dr. Fayad has been also extremely successful. He has trained over 40 postdoctoral fellows, clinical fellows and students. His trainees have received major awards, fellowships, and positions in academia and industry. In 2008, he received the Outstanding Teacher Award from the International Society of Magnetic Resonance in Medicine (ISMRM) for his teaching on cardiovascular imaging and molecular imaging. In 2009 he was awarded the title of Honorary Professor in Nanomedicine at Aarhus University in Denmark. Recently, he was one of opening speakers at the 2011 97th Scientific Assembly and Scientific meeting of the Radiological Society of North America (RSNA). In 2012, he was invited to give the Henry I Russek Lecture at the 45th Anniversary of the ACCF New York Cardiovascular Symposium. In 2013, he was elected Fellow of the International Society of Magnetic Resonance In Medicine, Magnetic Resonance Imaging, received a Distinguished Reviewer from Magnetic Resonance in Medicine and was selected as an Academy of Radiology Research, Distinguished Investigator In 2014 he received the Centurion Society award from his alma matter (highest award) Bradley University for his bringing national and international credit to his alma matter

He is married to Monique P. Fayad, MBA and is the proud father of Chloé (12 year old) and Christophe (8 year old) and after spending seven years in Manhattan now lives in Larchmont, runs in Central Park and participates regularly in New York Road Runners races. He also enjoys regular sailing and stand-up paddling in Larchmont, NY and beyond.
Nelly Alia-Klein, PhD
Associate Professor of Psychiatry
Associate Professor of Neuroscience
Co-chief, Neuropsychoimaging of Addiction and Related Conditions (NARC) Research Program
Icahn School of Medicine at Mount Sinai

Dr. Alia-Klein is Associate Professor of Psychiatry (primary) and Neuroscience (secondary) at the Icahn School of Medicine at Mount Sinai and co-chief of Neuropsychoimaging of Addiction and Related Conditions (NARC) research program.

Prior to joining Mt. Sinai, Dr. Alia-Klein was Medical Scientist at Brookhaven National Laboratory in New York where she developed a program of study on aggression. She received her PhD from Columbia University in New York City. Dr. Alia-Klein is Principal Investigator on NIMH R01 and co-investigator on several grants from NIDA. As co-chief of NARC, Dr. Alia-Klein works on gene-brain-behavior modeling to predict anger and reactive aggression in clinical diagnoses as Intermittent Explosive Disorder. One of her goals is to further develop understanding and treatment of anger attacks in psychiatric disorders. She published on the neurochemistry modulating these behaviors and the reactivity interplay of prefrontal and subcortical brain regions during provocation or other challenge. Her tools probe select genotypes and their effects on brain function through application of MRI and PET technology. Other topics of study such as sex differences are also of interest, in particular as they affect anger disorders.
Fred Lublin, MD
Professor of Neurology
Director, Corinne Goldsmith Dickinson Center for Multiple Sclerosis
Icahn School of Medicine at Mount Sinai

Dr. Lublin is the Saunders Family Professor of Neurology at The Icahn School of Medicine at Mount Sinai and Director of the Corinne Goldsmith Dickinson Center for Multiple Sclerosis at that institution. He received his medical degree in 1972 from Jefferson Medical College, Philadelphia, PA. He completed his internship in Internal Medicine from the Bronx Municipal Hospital, Albert Einstein Medical Center, and his residency at the New York Hospital, Cornell Medical Center.

As a neuroimmunologist, Dr. Lublin has a special interest in immune functions and abnormalities affecting the nervous system. He has been involved in both basic science and clinical research. He and his colleagues were among the first in the country involved with studies of Interferon beta-1b, which was approved by the Food & Drug Administration in 1993 to treat the relapsing-remitting form of Multiple Sclerosis. He is currently involved with several new clinical research protocols on promising agents for treating various aspects of MS. He was chairman of the National MS Society (USA) advisory committee on clinical trials of new drugs in Multiple Sclerosis and the National Multiple Sclerosis Society’s Research Programs Advisory Committee. He is a member of the National MS Society National Board of Directors and their medical advisory board. He is Chair of the New York City/Southern New York Chapter of NMSS Clinical Advisory Committee. He is a member of the International Medical & Scientific Board of the Multiple Sclerosis International Federation. Dr. Lublin and his colleagues at the National MS Society have re-defined the clinical course definitions of MS using data from a survey of the international MS community. He has chaired a task force on the ethics of placebo-controlled trials in MS. Dr. Lublin is a member of the international panel that periodically redefines the diagnostic criteria for MS. Dr. Lublin is co-chair of the National Institute of Neurological Diseases and Stroke MS Common Data Element committee and a member of their steering committee. He is a member of the WHO Advisory Group for the Revision of ICD-10 Diseases of the Nervous System working group on demyelinating diseases of the central nervous system. He is a Co-Chief Editor of the new journal Multiple Sclerosis and Related Disorders.
Dr. Lublin has published numerous scientific articles and belongs to many professional societies and advisory boards. Dr. Lublin has served as a consultant to the National Institutes of Health and to many pharmaceutical/biotech companies in all phases of new drug development and in preparation for presentation to the FDA and their advisory panels. He is the Principal Investigator of the NIH-sponsored multicenter Combination Therapy study in Multiple Sclerosis.
Dr. Xu is an Assistant Professor of Radiology at ISMMS. Dr. Xu has more than a decade long experience with MRI technical development and application, focusing on fMRI and diffusion MRI (dMRI) in the central nervous system. Before joining ISMMS, Dr. Xu was a key MRI sequence developer within the WU-Minn Human Connectome Project (HCP) consortium. He was instrumental for developing slice-accelerated multiband fMRI and dMRI sequences and for optimizing the HCP acquisition protocols, which have since seen widespread adoption in the neuroimaging community. His practical experiences during the WU-Minn HCP 3T and 7T protocol piloting, combined with his in-depth knowledge of the Siemens software and hardware platforms, allows him to contribute to BIC in numerous ways. These include leading the effort to disseminate the latest advances in fMRI and dMRI acquisition, pre-processing, analyses, and informatics (XNAT), developed within the WU-Minn HCP consortium, to the ISMMS neuroimaging community. Dr. Xu has received multiple awards including: International Society for Magnetic Resonance in Medicine M. S. Moore young investigator award finalist; National Multiple Sclerosis Society supported postdoctoral fellowship; International Progressive Multiple Sclerosis Alliance infrastructure award; Radiological Society of North America scholar award; and Brain & Behavioral Research Foundation (NARSAD) young investigator award. Dr. Xu’s recent interests focus on the development and clinical translation of reliable MR imaging biomarkers in the visual and sensorimotor pathways for multiple sclerosis and other neurological injuries.

Presentation: “Sinai BIC common imaging protocol.”

Harmonizing common MRI acquisition and analysis protocols holds great promise for studying the common neuroimaging features and its variability with sufficient power for neurological or psychiatric disorders across diagnostic domains. This talk highlights the efforts made so far by the BIC for an institutional-wide Sinai Common Imaging protocol to facilitate hypothesis generation and data-mining within the Sinai neuroimaging community.
Dr O’Halloran is an Assistant Professor of Radiology with a secondary appointment in Psychiatry at the Icahn School of Medicine at Mt Sinai. In addition to his supporting role in MRI acquisition and processing for the Brain Imaging Core (BIC) Dr O’Halloran is also a member of 2 research institutes at the Icahn School of Medicine: The Friedman Brain Institute (FBI) and the Translation and Molecular Imaging Institute (TMII). He also acts as the Chief of the Image acquisition core. Dr O’Halloran’s work centers around the development and application of novel MRI acquisition, reconstruction and post-processing methods, with a focus on Diffusion-Weighted Imaging (DWI). His initial work in diffusion was in developing rapid imaging techniques for measuring gas diffusion in the lung in order to study asthma on chronic obstructive lung disease. Since then his focus has shifted to high-resolution DWI in the brain to assess white matter structure and integrity. This work led to the development of novel high-resolution imaging methods in for the brain as well as motion correction techniques. At the Icahn School of medicine Dr O’Halloran is working on several DWI-related projects in clouding the application of DWI to the planning of deep brain stimulation, the study of white matter abnormality in addiction in the context of the NARC (Neuropsychomaging of Addiction and Related Conditions) study, white matter imaging in primates, and prospective motion correction for DWI as well as general MRI imaging.

**Presentation:** “Freeze that patient! Motion in (d)MRI and what we are doing about it.”

Subject motion is a leading cause of failed MRI exams, costing time, money, and potential harm to due delayed or missed diagnosis. Some estimates put the economic cost of motion at 200k per scanner per year. In this talk we explore the effects of motion on scans, solutions to these problems, and in particular, the methods available within BIC to deal with motion. We will also describe a planned project for prospective optical motion correction.
Dr. Kundu received his undergraduate degree (B.S. Chemistry) at Manhattan College, his Ph.D. from the University of Cambridge, and performed post-doctoral work at the NIH. His graduate training was supported by the NIH-Cambridge Scholars program, which facilitated graduate training at both Cambridge and NIH, in the labs of Drs. Ed Bullmore and Peter Bandettini, respectively. Dr. Kundu is an expert in the field of functional MRI (fMRI) analysis and denoising. He is currently an Assistant Professor in the Departments of Radiology and Psychiatry, and is involved in BIC activities relating to functional and structural brain imaging and BIC infrastructure and workflow design.

**Presentation:** “Studying resting state connectivity using multi-echo fMRI.”

This talk will discuss our going work development multi-echo fMRI methods and applications. Significant benefits of this approach include the ability to robustly study resting state connectivity and fMRI task activation under clinically-relevant constraints such as high subject motion, short scan duration, or small numbers of subjects. Application to the study of animal models will also be discussed.
Dr. Balchandani is an Assistant Professor of Radiology and Neuroscience at the Icahn School of Medicine at Mount Sinai. As the Director of the High Field MRI program at TMII, Dr. Balchandani focuses on developing novel techniques to exploit the power of high-field MR magnets to visualize the brain in unprecedented detail. She leads a team of 7T scientists to devise creative engineering methods to overcome some of the main limitations of operating at high magnetic fields, thereby enabling high-resolution whole-brain anatomical, spectroscopic and diffusion imaging as well as unlocking new contrast mechanisms and sources of signal. In order to achieve these goals, Dr. Balchandani’s team focuses on novel radio frequency (RF) pulse and pulse sequence design as well as specialized hardware solutions such as parallel transmission. These techniques are ultimately applied to improve diagnosis, treatment and surgical planning for a wide range of neurological diseases and disorders. Some clinical areas of focus for Dr. Balchandani’s team are: improved localization of epileptogenic foci; imaging to reveal the neurobiology of depression; and development of imaging methods to better guide neurosurgical resection of brain tumors. Dr. Balchandani is the recipient of a K99/R00 NIH Pathway to Independence Award from the National Institute of Neurological Disorders and Stroke for her grant entitled "High Resolution Magnetic Resonance Imaging and Spectroscopy of Epilepsy at 7T." She received her PhD in Electrical Engineering from Stanford University.

Presentation: “Exploring new ways to visualize the brain through 7T MRI.”

This talk will cover some of the recent technical advancements made by the ultrahigh field research team to improve high resolution anatomical, spectroscopic and diffusion weighted MRI of the brain at 7T. Application of these methods to improve imaging of epilepsy, brain tumors and psychiatric disorders will also be discussed.
Dr. Fan currently leads the Neuroimaging Laboratory at ISMMS. His laboratory combines functional magnetic resonance imaging with event-related potentials, genetics, physiological monitoring, and computational modeling to investigate the neuroanatomy and circuitry of cognitive and affective brain networks in healthy and psychiatric populations such as autism spectrum disorder.

**Presentation:** “Embodied mind: Physiological signals in functional MRI”

Functional magnetic resonance imaging (fMRI) techniques enable us to study brain activity during tasks and at rest. During fMRI, physiological signals that are from the body are typically viewed as a source of noise that obscure task-derived signals and therefore, recorded so that the impact of physiological responses can be mitigated during data analysis. However, bodily physiological responses, and by the extension, the autonomic nervous system that controls physiological outputs, are increasingly being recognized as key contributors to a lot of cognitive and affective processes in the brain. In this talk, I will discuss methods to record and incorporate the analysis of physiological indices in fMRI experiments, and share some of the findings from my lab on the role of physiological signals in brain activity.
Dr. Moeller is an Assistant Professor of Psychiatry and Neuroscience at the Icahn School of Medicine at Mount Sinai. He received his PhD in Psychology from the University of Michigan in 2010, where he studied conscious and unconscious determinants of behavioral and emotional self-control, and how these concepts could be applied to substance abuse. He then completed a NIDA-funded Postdoctoral Fellowship at Brookhaven National Laboratory to study addiction neuroimaging under the mentorship of Dr. Rita Goldstein and moved with her research team to Mount Sinai in 2013. His current research uses sensitive behavioral, imaging, and genetic paradigms to explore how drug-addicted individuals make drug-related choices, and to what extent such choices reflect deliberative, self-aware decisions or instead reflect a lack of insight into behavior or illness severity.

**Presentation:** “Neural correlates of drug choice in human addiction”

Individuals with drug addiction pursue and choose drug-related reinforcers over other pleasant, non-drug reinforcers, and the extent of such drug-related choice often correlates with addiction severity. While such drug-choice paradigms are readily accomplished in animal models and active human users, these paradigms are difficult to conduct in abstaining- or treatment-seeking individuals who, for ethical reasons, cannot be administered actual drugs. To address this challenge, our Lab developed tasks of simulated drug-choice that assess choice for drug cues (pictures) as a proxy of actual drugs. The current presentation describes some of this drug-choice research as well as our recent efforts to translate a similar picture-choice paradigm to fMRI.
Dr. Croxson is an Assistant Professor in the Departments of Neuroscience and Psychiatry at the Icahn School of Medicine at Mount Sinai. She has an M.A. in Natural Sciences from the University of Cambridge, and a M.Sc. and a Ph.D. in Neuroscience from the University of Oxford. Her work focuses on the role of the prefrontal and temporal cortex in cognition using non-human primate models. Currently, she has two main areas of research. First, she is interested in the functions of acetylcholine in memory and plasticity in the prefrontal and temporal cortex. Second, she investigates the effect of discrete brain lesions on the whole brain at the structural and functional level, using functional, structural and diffusion MRI, and combining it with behavioral studies.

**Presentation:** “Non-human primate imaging”

Recent advances have allowed us to acquire detailed imaging data from non-human primates in vivo. What value can such data provide when compared with the already high standard of images we can acquire from the human brain? One major contribution is that we can study the causal effect of targeted brain lesions on the whole brain in the same subjects, an opportunity that rarely arises in human patients. We are also able to investigate structural correlates of functional changes and validate them histologically. Finally, we can perform accurate comparative studies between the human and non-human primate brain. We are now able to acquire high-resolution structural, diffusion and resting-state functional MRI images from anesthetized rhesus monkeys to investigate these questions. I will describe studies using these multi-modal methods to investigate the relationship between structure and function in the non-human primate brain, and how it relates to the human brain.
Michael Michaelides, PhD
Postdoctoral Fellow
Department of Neuroscience
Icahn School of Medicine at Mount Sinai

Dr. Michaelides holds a Ph.D. degree in Biological Psychology from Stony Brook University. His graduate work was performed at Brookhaven National Laboratory and focused on behavioral neuropharmacology of addictive disorders and development of small animal PET/MRI methodologies. Since 2010, he is a postdoctoral researcher at Mount Sinai, working with Dr. Yasmin Hurd on behavioral, molecular, genetic, and epigenetic correlates of addictive disorders and on development of imaging methodologies for dissecting cell type-specific functional brain circuits in vivo. He has co-authored approximately 40 peer-reviewed publications utilizing small animal molecular imaging approaches. Dr. Michaelides has also co-founded two biotechnology companies that specialize in molecular imaging drug discovery/profiling services and on development of novel molecular imaging-based theranostics. His goal is to develop an independent research program combining translational use of in vivo molecular imaging technologies with cutting edge genetics, molecular biology and behavioral neuropharmacology techniques for studying the mechanistic basis of appetitive and mood and motivational disease.


The mammalian brain is a complex organ with billions of heterogeneous cells whose local and long-range functional connections regulate behavior and physiology. Traditional in vivo approaches for mapping functional brain anatomy are largely invasive, non-molecular, and implemented on anesthetized or immobilized animals. To overcome these limitations, we recently developed methodologies that enable non-invasive, dynamic, quantitative, high-resolution, molecular, whole-brain assessments of cell type-specific functional anatomy in freely-moving animals. These approaches fill a technological niche providing unbiased, direct, quantitative, molecular, and longitudinal information on whole-brain functional anatomy and thus can be used as an important reverse-engineering research strategy to dissect cell type- and in vivo-specific neuronal networks associated with normal as well as pathologic behavior.
Dr. Matilde Inglese is an Associate Professor of Neurology, Radiology and Neuroscience at the Icahn School of Medicine at Mount Sinai and Director of Neurology Imaging Research Program. Her current research, supported by the National Institute of Health and by the National Multiple Sclerosis Society focuses on the development and application of multimodal imaging techniques at high and ultra-high field strength to investigate the underlying pathological substrates of disease progression and accumulation of disability in multiple sclerosis and other neurodegenerative diseases. Dr. Inglese serves as a member for the National Institute of Health study sections and she is author of several original contributions published in the neurological and radiological scientific literature.

**Presentation:** “Dissecting multiple sclerosis heterogeneity: Insights from molecular and metabolic imaging”

Multiple sclerosis (MS) is an inflammatory/demyelinating and neurodegenerative disease of the central nervous system that affects young adults preferentially of female gender. Although the etiology of the disease is still unknown, MS is considered a multifactorial disorder likely caused by an interaction of environmental and genetic factors. The disease is highly heterogeneous from a clinical, pathological and immunological point of view thus limiting a precise prediction of long-term outcome and choice of optimal treatment. Conventional magnetic resonance imaging (MRI) is very sensitive to disease activity but lacks pathological specificity. Here we present a multimodality MRI approach developed to dissect the underlying pathological substrates of the disease (demyelination/neurodegeneration) progression and to identify the molecular substrates of physical and cognitive disability.
Lazar Fleysher, PhD
Associate Scientist
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Presentation: “Intracellular sodium quantification in the human brain using MRI”

In vivo sodium magnetic resonance imaging (MRI) provides a measure of the tissue sodium content in living human brain, but current methods do not allow non-invasive quantitative assessment of intracellular sodium concentration (ISC) – the most useful marker of tissue viability. I will present the first non-invasive quantitative in-vivo measurement of the ISC and of the cell volume fraction (CVF) in the healthy human brain made possible by measuring the tissue sodium concentration (TSC) and the intracellular sodium molar fraction (ISMF) at ultra-high field MRI. The method features the use of single-quantum (SQ) and triple-quantum filtered (TQF) imaging at 7 Tesla to separate intracellular and extracellular sodium signals and to provide quantification of ISMF, ISC and CVF. This novel method opens many possibilities for structural and functional metabolic studies in the healthy and diseased brain.
Dr. Mary Sano is Professor of Psychiatry and the Director of the Alzheimer's Disease Research at Mount Sinai School of Medicine. She is also the Director of Research and Development at the Bronx Veterans Administration Hospital. Currently she is the director of a national multi-center study known as CLASP (Cholesterol Lowering in Alzheimer’s Disease to Slow Progression). Dr. Sano is a neuropsychologist by training and has been involved in designing and conducting clinical trials for Alzheimer’s disease, Parkinson’s disease, and mild cognitive impairment of aging.

**Presentation:** “Imaging in dementia diagnosis and clinical research”
Sophia Frangou, MD, PhD  
Professor of Psychiatry  
Chief, Psychosis Research Program  
Icahn School of Medicine at Mount Sinai

Dr. Frangou, a leading expert in schizophrenia and bipolar disorders, joined to Mount Sinai in 2013. She has since established a clinical and translational psychosis program to rapidly expand research in genetics, neuroimaging, and neurobiology and transfer clinical relevant findings into clinical care. Her research of the neural pathways of disease expression, vulnerability, and resilience, along with associated genetic risk factors represents a paradigm shift in refining conceptual models for psychosis. Dr. Frangou previously worked as Head of the Section of Neurobiology of Psychosis at the Institute of Psychiatry in London and as a psychiatrist at the Maudsley Hospital.

**Presentation:** “A systems neuroscience perspective of schizophrenia and bipolar disorder”

Neuroimaging studies have generated a large body of knowledge regarding the neural correlates of schizophrenia (SZ) and bipolar disorder (BD). However, the initial goal of identifying disease-specific topographical mappings to localized brain regions or to distinct neural networks has not materialized and may be untenable. This talk will present evidence in support of a systems neuroscience approach. This evidence covers (a) brain structural, functional, and connectivity alterations and their implication for the clinical and cognitive manifestations of SZ and BD, (b) the prevailing system neuroscience models of the 2 disorders, and (c) key strategies likely to produce new insights into the mechanisms of underlying psychotic disorders and current plans to implement them at Mount Sinai.
Dr. Newcorn is a highly regarded clinician - researcher with special expertise in the areas of ADHD, aggression and child and adolescent psychopharmacology. He has been a member of the steering committee of the NIMH-funded multicenter study “Multimodal Treatment of Children with ADHD (MTA).” He was the primary investigator on an NIMH-funded ADHD Research Infrastructure Network devoted to understanding the neurobiology of ADHD, and is the principal investigator or co-investigator on several NIMH-funded and industry-funded grants that examine the clinical presentation and neurobiological basis of ADHD and its treatment. A nationally recognized educator and an editorial board member of several leading child psychiatry and psychology journals, Dr. Newcorn has studied many of the newer medication treatments for ADHD. He has published over 250 peer-reviewed articles and book chapters on these and related subjects. Dr. Newcorn’s most recent research focuses on the clinical and neurobiological basis of differential response to ADHD treatments, utilizing data obtained from clinical, neuropsychological, pharmacogenetic and fMRI measures.

**Presentation:** “Using fMRI to understand therapeutic mechanisms of ADHD medications”

Dr. Newcorn will briefly review the clinical presentation and neurobiological basis of ADHD, and present the results of several studies conducted at Mount Sinai that have examined the mechanisms of action of stimulant (e.g., methylphenidate, lisdexamfetamine), and non-stimulant (at oxoxetine, guanfacine) treatments. Findings indicate that stimulants affect brain regions within the prefrontal cortex (PFC), basal ganglia, limbic system and default mode network - resulting in improved inhibitory control, reward processing and emotion regulation. Non-stimulants have primary effects in PFC, with resultant improvements in cognitive control and top-down regulation of emotion processing. There is evidence for both common and unique effects of stimulant and non-stimulant medications, which offers potential for the development of personalized care.
James Murrough, MD
Assistant Professor of Psychiatry
Assistant Professor of Neuroscience
Icahn School of Medicine at Mount Sinai

Dr. James Murrough is Assistant Professor of Psychiatry and Neuroscience and Associate Director of the Mood and Anxiety Disorders Program at the Icahn School of Medicine at Mount Sinai. Dr. Murrough received his Bachelor of Science in neuroscience and behavioral biology from Emory University in Atlanta and his Medical degree from Tufts University School of Medicine in Boston. He completed his residency training in Psychiatry at Mount Sinai and a research fellowship in experimental therapeutics and clinical neuroscience in mood disorders, also at Mount Sinai. Dr. Murrough conducts clinical and translational research focused on identifying alterations in neurocircuitry and neurochemistry underlying mood and anxiety disorders. The overall goal of this program of research is to increase the understanding of mechanisms of illness in these disorders in order to identify novel, more effective treatments for patients.

**Presentation:** “Defining neuroimaging biomarkers of depression and rapid antidepressant treatment response”

This presentation will briefly review the state of the science regarding neuroimaging biomarkers for depression. New results from functional MRI studies of ketamine in patients with treatment-resistant depression will be presented. These results will be discussed with an emphasis what these findings can teach us about depression and the prospects for neuroimaging biomarker utilization for therapeutic development.
Dr. Koenigsberg is Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai and Co-Director of the Mood and Personality Disorder Research Program at Mount Sinai Medical Center. He is on the staff of the James J Peters VA Medical Center. Dr. Koenigsberg’s research is focused on the neurobiological correlates of the social, affective and cognitive disturbances which characterize the personality disorders. He is employing functional neuroimaging to study implicit and explicit mechanisms of emotion regulation and social interaction in borderline personality disorder and avoidant personality disorder patients. He is currently conducting a study to determine whether borderline patients can be trained to enhance their emotion regulatory abilities and normalize their neural processing with mental strategies that could be incorporated into psychotherapeutic treatments. He is also exploiting economic exchange game methods to examine the phenomenology and neural correlates of interpersonal interaction in BPD. Dr. Koenigsberg has been recipient of four NIMH R01 research grant awards. He also completed graduate study in high-energy physics.

**Presentation:** “Mechanisms of dysregulated emotion and re-establishing emotional control in borderline personality disorder”

Emotional dysregulation is a core feature of many forms of psychopathology, leading to extreme emotionality. Borderline personality disorder (BPD), a prevalent and difficult to treat disorder with high morbidity and substantial suicide risk, is the prototypical disorder of emotion dysregulation. We will present imaging data demonstrating anomalies in neural activity in BPD compared to healthy subjects as they engage the emotion regulation mechanism cognitive reappraisal. We will present behavioral and neural evidence suggesting that BPD patients can be trained to enhance their ability to employ cognitive reappraisal to decrease negative emotional reactions to aversive stimuli.
Dr. Gabbay is the Chief of the Pediatric Mood and Anxiety Disorders Program at the Icahn School of Medicine. Her research has focused on the neurobiology and phenomenology of pediatric mood disorders, using a multidisciplinary approach combining immunological, functional MR imaging (fMRI), and MR spectroscopy.

**Presentation:** “Neuroimmunology of reward processing and anhedonia in adolescents”

Dr. Gabbay will present data assessing the neurochemical and neurocircuitry alterations that are associated with the clinical symptom of anhedonia, the reduced capacity to experience pleasure.
Gold nanoparticle-ligand contrast agents for sub-micron imaging of synaptic features

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Our ability to better understand neurological disease progression and measure the connectome accurately is hampered by the lack of safe, non-destructive, non-invasive in vivo imaging tools. MRI and PET imaging do not provide the sub-micron resolution needed to image receptor densities or create intricate maps of neural circuitry. In addition, in vivo contrast agents presently used are limited by their specificity, uptake, resolvability, and clearance.

Using functionalized gold nanoparticles, nanoCT can provide 1,000-fold better resolution than current MRI and PET imaging techniques and allows for imaging of new features. Gold nanoparticles have proven to be safe, can be functionalized to cross the blood brain barrier via receptor mediated endocytosis, are easily cleared, and can be conjugated to a variety of validated affinity ligands. Presented here is our current work on highly-specific nanoCT neurological contrast agents. We hypothesize that development of such reagents can provide a route to quantitatively measure neurotransporter and neuroreceptor distributions non-invasively and non-destructively.
Trait differences and precuneus involvement in reactive aggression

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Reactive aggression occurs in response to provocation and culminates in recurrent bouts of anger in intermittent explosive disorder (IED). To improve our understanding of neural underpinnings of reactive aggression, we compared brain responses during aggressive responding and following provocation in reactive-aggressive (RA) and non-aggressive (NA) participants using the functional MRI-adapted Point-Subtraction Aggression Paradigm (PSAP).

Eleven male RA (5 IED, 6 subthreshold-IED) were matched with eleven male NA on race, education, and age. Participants completed psychiatric interviewing, personality questionnaires, and performed the fMRI-PSAP against a fictitious opponent who infrequently provoked the participant. In each fMRI-PSAP trial, participants could choose between increasing their earnings (monetary gain option), or retaliating by taking away money from their opponent (aggressive option, no monetary gain).

Compared to NA participants, RA participants reported elevated trait anger and negative emotionality (\(p_s<.001\)), but were not more aggressive during the PSAP (\(p>.32\)). Nevertheless, in comparison with NA participants, RA participants exhibited increased brain responses in the precuneus and decreased brain responses in the left anterior insula/putamen when retaliating relative to increasing their earnings (aggressive vs. monetary option, Figure 1). Interestingly, brain responses were decreased in the precuneus in RA participants in monetary trials with a preceding provocation versus no provocation (Figure 1).

Our findings suggest that the precuneus, an important functional node in the default mode network, is not only involved in aggressive people during rest (cf., Alia-Klein et al, 2014), but also during functional tasks eliciting aggressive behavior in congruence with their traits.
Central Control of the Autonomic Nervous System

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Many behavioral disorders, including autism spectrum disorder, schizophrenia, general anxiety disorder, attention deficit disorder, and psychosis, may involve a fundamental deficit in the processing of internal (visceral) and external (sensory) stimuli. Core deficits in the processing of autonomic nervous system (ANS) signals may cause tonic and/or reflexive autonomic dysfunctions of these disorders, and may contribute to social and behavioral deficits. A better understanding of central autonomic networks may provide greater insight into the neuropathology of behavioral deficits in these disorders.

This study aims to identify the neural networks associated with the central control of autonomic regulation and the influence of these networks on mental processes by integrating functional magnetic resonance imaging and physiological monitoring during rest and behavioral tasks. We examined the network-level connectivity patterns attributed to physiological fluctuations at baseline (rest), during sensorimotor processes, and during higher-order behavior with a socioemotional task in neurotypical adults between 18-39 years old (n=20). We found that various regions of the cingulate cortex were commonly recruited in each task and that connectivity between the cingulate cortex and other subcortical structures implicated in ANS regulation were context-dependent.

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Neural Correlates of Self-Perceptions in Adolescents with Depression

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Adolescence is a critical period in which the sense of self and its supporting neural structures develop. Cortical midline structures that are part of the default mode network (DMN) have been found to subserve self-referential processing, and these regions are hyperactive in depressed adults. However, little is known about the neural structures underlying self-referential processing in depressed adolescents, who are at this critical stage for self-formation.

Twenty adolescents with depression and 19 healthy controls underwent fMRI scanning. Participants were asked if positive and negative traits described themselves (self), were a good trait (general), or contained the letter e. ANCOVAs and correlations assessed relations between groups, trait valence, and category (self, general).

Behaviorally, depressed adolescents showed a less positive self-perception than healthy controls. Depression severity was negatively correlated with positive self-ratings. Neuroimaging analyses revealed that depressed adolescents showed greater activity in the precuneus for all judgments. Both groups showed activity in the medial prefrontal cortex and precuneus in response to negative traits.

Given that depressed adolescents showed hyperactivity in the precuneus and depression severity was also associated with reduced positive self-perception, it is possible that preoccupation with worse perceptions may be driven by over activity within the DMN.

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Heuristic MRI Landmarks of Human Habenula

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ISMMS ¹Radiology, ²Neurosurgery, ³Pediatrics, ⁴Pathology, ⁵SUNY Stony Brook Psychiatry and Neuroscience

The habenula (Hb) is an important structure related to aversion and reward system regulation. However, in vivo investigation of human Hb has been limited by its small size, coupled with a lack of histologically validated in vivo localization criteria. In this ex vivo MRI and histology study, we will explore MR contrasts and histological evidence of: (i) boundaries between the medial habenula (MHb), lateral habenula (LHb), and dorsalmedial thalamus; (ii) margins between medial and lateral subdivisions of the LHb; and (iii) the asymmetry of the Hb nucleus. We will also derive heuristic anatomical MRI landmarks, supported by histology, and examine inter-subject variability to assess their use for in vivo localization.

Human brain tissue samples were fixed in formalin and transferred to phosphate-buffered saline (PBS). Preliminary images (Fig. 1) were obtained on a 7T human whole-body scanner [Siemens, Erlangen, Germany] with 1Tx/32Rx head coil [Nova Medical, USA] using predominantly proton density weighting to distinguish among different deep grey matter tissues: TR/TE=59/4.25 ms, flip angle=8 deg., 3D gradient echo sequence, 400 µm isotropic resolution, ~ 20 min.).

Histological slides will be obtained from the same specimen in the same orientation as the ex vivo MRI slices. Histological staining will be performed on both large slices and embedded pieces: (H&E, myelin, and iron stains) to make direct comparison of MRI and histological specimens.

Fig.1: (A) Ex-vivo proton density weighted image at 400 µm isotropic resolution from 7T and (B) atlas image from the Allen Brain Institute showing the Hb nucleus (blue arrows). Neurobiological Basis of Response to Lisdexamfetamine in Adults with ADHD
Recent evidence implicates motivation-reward mechanisms in the pathophysiology of ADHD. The objective of this study was to determine the effects of Lisdexamfetamine (LDX) on the brain motivation-reward system.

Twenty adults with ADHD (age: 19-52, 11 males) were treated with LDX and Placebo in a randomized, cross-over design. Subjects were scanned twice, after 3–5 weeks on either No drug/Placebo or LDX, using a passive-avoidance learning task. ADHD-RS scores were collected. The blood-oxygen-level-dependent (BOLD) signal was modeled using regressors for the images at the time of the decision (chosen vs. refused), and when feedback was given (reward or punishment). Decision-related regressors were weighted by subject expectation, and outcome-related regressors were weighted by the prediction error.

LDX increased the modulation of the BOLD responses by the expected value in the precuneus and lateral orbitofrontal when choosing to respond, and in dIPFC, when refusing to respond. Also, LDX increased BOLD response in the ventral striatum, when a reward was received, and increased the modulation by prediction error in vmPFC. Increased activation in ventral striatum and vmPFC was positively correlated with clinical improvement.

These findings suggest that LDX may act by increasing sensitivity in the motivation-reward system, which is thought to be compromised in individuals with ADHD.
Neural Responses to Positive Emotion are Associated with Perceived Stress in Patients with Major Depressive Disorder

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Functional MRI (fMRI) analysis can help highlight neural circuitry involved in major depressive disorder (MDD). Patients with MDD underwent fMRI and completed self-reports of perceived stress in their lives in order to determine neural correlates of stress perception. One measure is the Perceived Stress Scale (PSS), a self-report measuring patient perception of stress.

15 participants with MDD (ages 23 to 68, 7 female) completed a positive emotion identification task during fMRI. Using whole-brain general linear modeling and correlation analyses, we identified brain regions where the change in the Blood-Oxygenated-Level-Dependent (BOLD) signal during positive emotion perception is associated with perceived stress.

Neural responses to positive emotion within the thalamus and cerebellum were negatively associated with perceived stress (whole brain FWE corrected, p<0.05). Higher neural activation in response to positive emotion correlated with less perceived stress. The thalamic cluster of interest extended into the precuneus, the dorsal cingulated gyrus, and the insula, with the most robust finding in the pulvinar thalamus (mean correlation = -0.59).

These results suggest that brain systems involved in processing positive emotion influence the subjective perception of stress.

(Funding: National Institutes of Mental Health, ISMMS)
Evidence suggests the habenula (Hb) plays an important role in depression. Projections from the Hb inhibit the reward system through modulation of midbrain dopaminergic and serotonergic signaling. However, the small size of the human Hb limits in vivo investigation via standard neuroimaging methods. In the present pilot study, we aim to address this challenge by examining Hb connectivity using high-resolution resting-state fMRI (rsfMRI).

Subjects (N=7) underwent 15-minute rsfMRI scans at 3T and 7T using 32-channel head-coils. Isotropic high-resolution multiband-accelerated gradient-echo EPI images of 2.1mm³ (3T, one run), 1.6mm³ (7T, two runs), and 1.28mm³ (7T, two runs) were acquired, preprocessed using Human Connectome Project pipelines, and analyzed via the CONN toolbox using anatomically-derived Hb seeds (Fig1).

Consistent connectivity patterns of Hb seeds for each individual were observed at 3T with the contralateral Hb, bilateral insula, and thalamus (Fig2). More widespread patterns, including connectivity with the midbrain and prefrontal cortex, were evident for some subjects (Fig3). Results were corroborated in the same subjects at 7T with exquisite spatial specificity to grey matter.

These preliminary findings demonstrate the ability to detect Hb connectivity, including expected midbrain connections, using high-resolution 3T rsfMRI, and the improved spatial specificity of ultra-high-resolution 7T rsfMRI. Confirmation of patterns obtained from this small sample will require additional subjects.

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Learning can be guided by unexpected success or failure, signaled via dopaminergic positive (+RPE) and negative reward prediction error (–RPE) signals, respectively. Despite limited empirical evidence, RPE signaling is thought to be impaired in drug addiction. To fill in this gap, we studied the feedback negativity (FN) that is sensitive to both reward and the violation of expectation as a measure of RPE. We examined the FN in 25 healthy controls, 25 individuals with cocaine use disorder (CUD) who tested positive for cocaine on the study day (CUD+), indicating cocaine use within the past 72h, and in 25 CUD who tested negative for cocaine (CUD–). Participants performed a gambling task predicting if they would win/lose money on a trial-by-trial basis given three known win probabilities (25%, 50%, or 75%). FN was scored for the outcome in each trial. A significant interaction between prediction, outcome and group revealed that controls showed increased FN to unpredicted compared to predicted win (intact +RPE) and decreased FN to unpredicted compared to predicted loss (intact –RPE). However, neither CUD subgroup showed FN modulation to loss (impaired –RPE), and unlike CUD+, CUD– also did not show FN modulation to win (impaired +RPE). Thus, using the FN, the current study directly documents –RPE deficits in CUD (an impaired +RPE was observed in CUD– only). Results highlight the significance of studying the mechanisms underlying –RPE signaling in addiction, which may help clarify the persistence of drug use despite repeated unfavorable life experiences (e.g., incarceration) in CUD.

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Neural Effects of Social Skills Treatment on Eye Gaze Processing in Autism

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Social deficits are a hallmark of ASDs and have been associated with underactivity in brain regions important for social cognition. Social skills training using a cognitive-behavioral (CBT) approach has been shown to improve social behavior in children with ASDs. However, little is known about the neural response to treatment. We examined the neural effects of CBT social skills groups on eye gaze processing in children with ASD. Verbally fluent children (ages 8-11) were randomized to CBT or facilitated play comparison group. Behavioral assessments and fMRI were conducted at baseline and endpoint (12 weeks). While undergoing fMRI, children viewed emotionally expressive faces with direct or averted gaze. Following treatment, the CBT group showed greater activity in the medial prefrontal cortex (MPFC) and ventrolateral PFC (VLPFC) relative to baseline (Figure 1). In contrast, the comparison group did not show any regions of increased activity. When directly comparing the two groups, the CBT group showed greater increases in the MPFC, implicated in theory of mind, relative to comparison (Figure 2). Furthermore, greater increases in MPFC and VLPFC activity following treatment were associated with older baseline age for the CBT group. Findings suggest that a cognitive-behavioral approach to social skills treatment may increase activity in social brain networks, contributing to our understanding of the plasticity of networks involved in social cognition.

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Brain activity associated with impairment of motor imagery in patients with multiple sclerosis

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Motor imagery (MI) is defined as mental movement execution in the absence of actual movement and involves neural networks which overlap with those activated during actual motor execution (ME). A recent behavioral study has shown that MI is impaired in multiple sclerosis (MS) patients.

Seventeen patients with clinically isolated syndrome (CIS), 17 patients with relapsing-remitting (RR) MS and 17 healthy controls (CTRLs) underwent behavioral testing and MRI. High-resolution T2- and T1-weighted images were acquired for anatomical localization. Functional MRI was acquired first during rest and then during block-design ME (squeezing a ball with the dominant/non-dominant hand) and MI of the same movement. Whole-brain analysis of MI and ME data was performed with a GLM approach using FSL and groups were compared for each task. A group ICA analysis was performed on the rest fMRI data using temporal concatenation. Individual default mode and sensorimotor networks were obtained using dual-regression and compared using non-parametric permutation testing as implemented in randomise.

Overall, patients recruited more extensive areas during both ME and MI (Fig.1), which was impaired in both patient groups (anisochrony). The sensorimotor network was significantly altered in RR-MS compared to CTRLs. Next steps should explore the connectivity changes within the motor network related to the observed anisochrony and association with resting state activity.
Using resting state fMRI to evaluate functional connectivity as a predictor of resilience to social defeat in a mouse model: A pilot study

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Depression is often characterized by abnormalities in cortico-limbic circuitry. However, little is known about the neurocircuitry involved in predisposing individuals to developing depression following a stressor. The purpose of this pilot was to explore the feasibility of resting state functional magnetic resonance imaging (rs-fMRI), a minimally invasive method for measuring functional connectivity, for predicting stress response.

A cohort of mice (n=15) underwent rs-fMRI prior to social defeat (SD) stress, a well-established mouse model of depression. Following SD, the mice were classified into resilient or susceptible based on a social interaction (SI) score. Seed-based cross correlation for selected atlas-based cortical and subcortical regions was then correlated with the SI.

We observed a trend towards increased correlative activity between prefrontal and limbic regions in the more stress-resilient animals as compared with susceptible mice.

rs-fMRI is a viable minimally invasive method for the evaluation of the cortico-limbic functional connectivity as a predictor of resilience/susceptibility to SD.
fBIRN-X: an Updated Quality Assurance Protocol for Slice Accelerated fMRI

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Recent advances in slice accelerated (i.e., multiband) echo planar imaging (EPI), developed in the Human Connectome Project (HCP), have seen widespread adoption in the neuroimaging community. Emergent multi-center studies based on multiband techniques, as evidenced by the recent NIH Connectome Related to Human Diseases (U01) RFA, require a quality assurance protocol to ensure scanner stability and consistent, error-free multiband sequence implementation. The conventional fBIRN QA analysis, the fMRI community’s gold standard for more than a decade is limited in this new era of slice accelerated fMRI.

We propose an updated fBIRN QA protocol (fBIRN-X) to address the lack of cross-slice QA metrics in the conventional fBIRN QA analysis. By examining both frequency and spatial domains of the signal within and across simultaneously excited and acquired slices, we are able to detect and quantify (i) signal leakage between simultaneously excited slices; (ii) slice cross-talk and banding artifacts; (iii) transmitter drift; and (iv) subtle spiking and power fluctuations detectable only through cross-slice analysis. fBIRN-X QA results from QA data collected by the WU-Minn HCP and Mount Sinai demonstrate the value and importance of these cross-slice QA metrics for multi-center studies.

Additionally, we show a cylindrical agar phantom designed for this QA protocol, which also contains structures for testing geometric distortions, as a replacement to the standard spherical fBIRN phantom for more accurate detection of scanner hardware or MB pulse sequence abnormalities.
Cognitive Function and DTI Tractography in Combat Veterans with Blast-Related Mild Traumatic Brain Injury

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Blast-related mild traumatic brain injury (mTBI) is associated with a variety of neuropsychological impairments, most notably in attention, memory and executive function. However, mechanisms of brain damage and cognitive impairment after blast exposure are not fully understood.

We examined cognitive function and its relationship to DTI fractional anisotropy (FA) in blast-exposed veterans with (n=24) and without (n=16) a diagnosis of mTBI. We assessed differences in neurocognitive measures as well as differences in white matter (WM) integrity, using t-tests and MANOVA respectively. We also examined the association between WM integrity and cognition across the entire blast-exposed population.

We found no significant difference between mTBI and controls in FA in WM tracts. Neurocognitive performance significantly correlated with a number of WM regions with mTBI's performing worse on measures of attention/processing, executive function, and memory.

The lack of differences in FA in our subjects may be because all subjects were blast-exposed. Future work will include non-exposed controls. Elucidating the roles of blast exposure and TBI on cognition is crucial for effective treatment planning.

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Differing Amygdala-Frontal Functional Connectivity Abnormalities in Borderline and Schizotypal Personality Disorders

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Aberrant connections between the amygdala and frontal brain regions may contribute to emotional and behavioral dysregulation exhibited in borderline personality disorder (BPD), yet neural connectivity in BPD remains poorly understood. Additionally, amygdala-frontal connectivity in schizotypal personality disorder (SPD) has yet to be investigated. The present study examined amygdala connectivity during habituation to pleasant, unpleasant, and neutral images in BPD, SPD, and healthy control (HC) individuals.

Patients were unmedicated at the time of their scan. During fMRI, BPD (n=33), SPD (n=28) and HC participants (n=32) viewed a series of intermixed pleasant, neutral, and unpleasant pictures, each presented twice within their respective trial block. Hand-traced left and right amygdala regions-of-interest were used as seeds for each participant in wholebrain connectivity analyses using FSL software. Between-group differences in amygdala connectivity were examined for novel and repeated pictures in each of the three conditions.

Compared to HCs, the BPD group exhibited increased connectivity while the SPD group showed decreased connectivity between the left amygdala and the frontal lobe and anterior cingulate gyrus during unpleasant pictures. Additionally, compared to HCs, the SPD group exhibited increased connectivity between the right amygdala and the frontal lobe and anterior cingulate gyrus. During pleasant images, the BPD group showed increased connectivity between the right amygdala and the frontal lobe in comparison to the SPD group, but did not significantly differ from HCs.

These results suggest distinct patterns of dysfunction in amygdala-frontal connectivity in individuals with BPD and SPD. Clinical symptom correlates will also be presented.
Comorbid alcohol use among cocaine users is common. Alcohol use and cocaine use separately are associated with neuropsychological dysfunction. Here, we tested their combined effects on verbal memory and gray matter volume (GMV).

Matched participants [25 individuals with cocaine use disorder (CUD) with heavy alcohol use (CUD-A); 21 CUD with light alcohol use (CUD-L); and 22 Controls] were administered the California Verbal Learning Test (CVLT-II) and underwent structural MRI. We compared the groups on CVLT-II, drug use, and GMV with voxel-based morphometry (VBM).

CUD-A, relative to CUD-L and Controls, showed lower correct- \( p=0.03 \) and long-delay \( p=0.02 \) free recall on the CVLT-II; and lower bilateral hippocampal \( p=0.009 \) and left lingual \( p<0.001 \) GMV. Across participants, higher bilateral hippocampal GMV correlated with more words recalled and later age of alcohol use onset (Fig. 1); and better delayed recall correlated with higher left lingual gyrus GMV and fewer years of heavy drinking (Fig. 2).

Individuals with a history of cocaine and heavy alcohol use demonstrate impairments in verbal memory relative to cocaine users who do drink lightly. As CVLT performance varied by duration of alcohol use, and CUD-L did not differ from controls in CVLT-II performance, it is possible that alcohol use drives these deficits in CUD.
The neural mechanisms of anticipation and implementation of reappraisal in avoidant personality disorder patients

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Avoidant personality disorder is characterized by pervasive anxiety in anticipation of and during exposure to social situations. An important but underexplored question concerns whether anxiety in avoidant patients is associated with an impaired ability to engage emotion regulatory strategies before and during appraisal of negative social stimuli.

We addressed this question by examining the neural mechanisms underlying the use an adaptive emotion regulation strategy, reappraisal. Amygdala activity, associated with negative emotion reactivity, was of particular interest. We measured neural activity via functional magnetic resonance imaging both in anticipation of and during performance of an image-based reappraisal task in 17 avoidant patients and 21 healthy participants.

Relative to healthy participants, avoidant patients showed pronounced amygdala hyper-reactivity during reappraisal anticipation. Further, in avoidant patients this hyper-reactivity effect was positively associated with increasing self-reported anxiety levels. No group differences in reappraisal-related activity were identified.

These results suggest that amygdala reactivity may represent a key component of the neural mechanisms underlying the heightened anxiety present in avoidant patients.

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