

## Neuroscience

J. John Mann, M.D, Chief

### *Brain Imaging*

Ramin V. Parsey, MD, PhD, Research Psychiatrist II  
Ronald Van Heertum, MD, Medical Specialist II  
Ashish Ojha, PhD, Research Scientist II  
Kjell Erlandsson, PhD, Assistant Professor of Clinical Neuroscience (in Psychiatry & Radiology)  
Maté Milak, MD, Assistant Professor of Psychiatry  
R. Todd Ogden, PhD, Research Scientist IV  
Peter Freed, MD, Postdoctoral Research Fellow  
Malingham Pradhaban, M.S., Research Scientist II

### *PET Chemistry*

J.S. Dileep Kumar, PhD, Research Scientist V  
Norman Simpson, B.S., Research Scientist IV  
Jaya Prabhakaran, PhD, Associate Research Scientist  
Vattoly Majo, PhD, Associate Research Scientist

### *Computer Systems*

Joseph Grun, B.S., Research Scientist II  
Eli Kunstlinger, B.A., Officer of Administration / Senior User Services Consultant

### *Neuroscience Research Clinics*

Maria A. Oquendo, MD, Research Psychiatrist II  
Ainsley Burke, PhD, Research Scientist II  
Dianne Currier, PhD, Senior Staff Associate  
Elizabeth Sublette, MD, Research Fellow  
Gregory Sullivan, MD, Assistant Professor of Clinical Psychiatry  
Jill Harkavy-Friedman, PhD, Research Scientist IV  
Michael Grunebaum, MD, Research Psychiatrist II  
Sari Trungold, PhD, Research Scientist I

### *Personality Disorders*

Barbara Stanley, PhD, Research Scientist VI  
Beth Brodsky, PhD, Research Scientist II  
Scott Wilson, PhD, Research Scientist I  
Eric Fertuck, PhD, Postdoctoral Research Fellow  
Leo Sher, MD, Research Psychiatrist I

### *Neuropsychology*

John Keilp, PhD, Research Scientist IV  
Marianne Gorlyn, PhD, Postdoctoral Research Scientist

### *Neuropharmacology*

Hadassah Tamir, PhD, Research Scientist VI  
Kuo-peing Liu, M.S., Research Scientist IV  
Shu-chi Hsiung, M.S., Research Scientist III

### *Developmental Disorders*

Martha Welch, MD, Assistant Clinical Professor in Psychiatry

*Molecular Neuroanatomy*

David Ruggiero, PhD, Professor of Clinical Neuroscience (in Psychiatry)  
Muhammad Anwar, M.S., Senior Staff Associate

*Neurophysiology and Small Animal Models*

Mark Underwood, PhD, Research Scientist V  
Loubna Erraji-Benchekroun, PhD, Instructor in Clinical Neuroscience

*Molecular Biology and Behavior*

Claudia Schmauss, MD, Research Scientist V

*Neurophysiology*

Stephen Rayport, MD PhD, Research Psychiatrist II  
Nao Chuhma, MD PhD, Research Scientist III  
Takeo Mizuno, MD PhD, Associate Research Scientist

*Molecular Recognition*

Jonathan Javitch, MD, PhD, Research Scientist VI

*Neurotransmitter Regulation*

David Sulzer, PhD, Research Scientist V

*Chemical Neuroanatomy and The Diane Goldberg Laboratory for Molecular Imaging of Neural Disorders*

Victoria Arango, PhD, Research Scientist VII  
Helene Bach-Mizrachi, PhD, Instructor in Clinical Neuroscience  
Jason Scalia, PhD, Instructor in Clinical Neuroscience  
Mihran Bakalian, B.A., Research Scientist II  
Suham Kassir, B.S., Research Scientist III  
Yan Liu, MD, Research Project Manager I

*Neuropathology*

Andrew Dwork, MD, Research Pathologist II  
Branislav Mancevski, MD, Associate Research Scientist  
Gorazd Rosoklija, MD, PhD, Associate Professor of Clinical Psychiatry

*Human Genetics and Neurochemistry*

Yung-yu Huang, M.S., Research Scientist IV  
Fatemeh G. Haghighi, PhD, Research Scientist VI

*Statistics and Data Management*

Steven Ellis, PhD, Research Scientist V  
David Andrews, M.A., Officer of Administration / Information Systems Analyst  
Hanga Galfalvy, PhD, Assistant Professor of Clinical Neuroscience (in Psychiatry)  
Adrienne Tin, M.S., Project Administrator

## *Administration*

Renee Azima Heller, M.A., Project Administrator IV  
Nancy Geibel, M.S., Project Administrator III  
Christine Pierson, Administrative Support Assistant III  
Nayris Sanchez, Administrative Clerk  
Sana Bentebbaa, Administrative Support Assistant II

## **Overview**

The Division of Neuroscience spans the research spectrum from basic cell biology to *in vivo* imaging, molecular genetics and treatment trials. It emphasizes translational research and employs a multidisciplinary approach to psychiatric research to examine the biological substrate of mental illness at multiple levels. The Division has historically comprised three sub-divisions. The *Neurochemistry SubDivision* spans basic molecular recognition studies to treatment studies. The *Neuropathology SubDivision* conducts neuroanatomical mapping, quantitative morphometric and gene expression studies in human, nonhuman primate and rodent brains, postmortem brain studies of psychiatric disorders and provides neuropathology services to the New York State Office of Mental Hygiene (OMH). It maintains an archival collection (brain bank) of these specimens as well as other brain specimens collected for research purposes. The *Brain Imaging SubDivision* conducts functional and structural brain imaging studies in rodents, baboons and human subjects. This subdivision develops novel PET ligands for monoamine receptors, enzymes and transporters, amyloid protein and peptide receptors. It studies disease processes, effects of gene variants and childhood adversity on brain biology, biologic predictors of treatment outcome and the use of biomarkers for studies of drug effect and the relationship of drug actions to occupancy of the hypothesized site of action.

The Division of Neuroscience is one of the largest at NYSPI and conducts a range of basic and clinical studies. It has four center grants. The NIMH-funded Silvio O. Conte Center for the Neuroscience of Mental Disorders: *The Neurobiology of Suicidal Behavior* (PI: John Mann) investigates risk factors for suicidal behavior in mood disorders, schizophrenia, and personality disorders. The Conte Center utilizes human postmortem studies and translational approaches such as novel PET tracers for brain imaging, new peptide assays in cerebrospinal fluid, and an investigation of candidate genes and basic biologic and cognitive endophenotypes. The Stanley Medical Research Institute's Center for the Applied Neuroscience of Bipolar Disorders (PI: John Mann) uses neurochemical postmortem studies to examine the neurobiology of bipolar disorders and to inform the design and goals of functional imaging studies in bipolar clinical studies. The third center is the Moody Center for the Study of Early Onset Bipolar Disorder, headed by Maria Oquendo. This center seeks to use functional MR and genetics to detect early onset bipolar disorder as a step towards preventative intervention. The fourth center is the NIMH funded Developing Center Suicide Intervention Center headed by Barbara Stanley.

## **Current Research**

### *Neurochemistry*

The major areas of clinical investigation for Neurochemistry have been the biological basis of mood, anxiety and psychotic disorders, the action of antidepressants and other psychotropics, and risk factors for suicidal behavior. Basic studies have involved studies of neurotransmitter systems and the action of antipsychotics and antidepressants.

The NIMH-funded Silvio O. Conte Center for the Neuroscience of Mental Disorders (PI: John Mann) supports studies into the risk factors for suicidal behavior in mood disorders, schizophrenia, and personality disorders. This work has defined a more comprehensive model of suicidal behavior based on clinical and biological findings from a large prospective study that utilizes novel PET tracers for brain imaging, new peptide assays in cerebrospinal fluid, candidate gene profiling and more basic endophenotypes of stress responsiveness.

The Stanley Medical Research Institute Center for the Applied Neuroscience of Bipolar Disorders uses PET scanning to study the neurochemistry of bipolar depression and the action of antidepressants and mood

stabilizers. Postmortem neurochemical studies inform the design of the functional imaging studies. The ultimate goal of the Stanley Center is to develop treatment selection guidelines based on *in vivo* neurochemical testing of bipolar patients.

Neuroscience Research Clinics/Neuropsychology/Personality Disorders: Dr. Maria Oquendo coordinates the clinical/biological studies in the Division. Drs. Michael Grunebaum, Leo Sher and Elizabeth Sublette conduct psychobiological studies of mood and psychotic disorders. Dr. Peter Freed studies mood regulation and grief process using fMR. Dr. Ainsley Burke trains and supervises the clinical evaluation core research staff and works on aspects of familial transmission of adversity. The studies of suicidal behavior in schizophrenia are directed by Dr. Jill Harkavy Friedman. Neuropsychological studies of cognitive function and impulsiveness in mood, psychotic and personality disorders are conducted by Dr. John Keilp. Dr. Barbara Stanley conducts neurochemical and psychological investigations in borderline personality disorder. One of her NIMH grants supports a parallel group, randomized, double blind study of the efficacy of a psychotherapy called dialectical behavior therapy versus an SSRI medication in the prevention of suicidal behavior in borderline personality disorder. Dr. Oquendo has an NIMH grant to conduct a double blind, randomized treatment study comparing lithium and divalproex maintenance treatment on suicidal behavior in bipolar disorder. Drs. Stanley and Oquendo head a Developing Center for Interventions to prevent suicide funded by NIAAA. Drs. John Mann, Maria Oquendo, and Ramin Parsey have developed methods using Positron Emission Tomography (PET) for quantifying binding to serotonin receptors. These techniques allow study of mood disorders, the effect of treatment with medication or ECT, and identification of high-risk patients and the localization of regional brain abnormalities in high-risk patients. These studies identify specific prefrontal cortical regions that determine lethality of suicidal behavior by mediating the degree of intent and impulsivity, which, in turn, determine the medical lethality of suicidal behavior. They have also mapped the brain regions with abnormal serotonin system function in depressed patients and identified regions of abnormality associated with specific components of psychopathology. The Family Center conducts studies of bipolar probands and their offspring and is headed by Dr. Maria Oquendo. Other studies examine genetic influences on the manifestation of suicidal and self-harming behaviors in collaboration with Drs. T. Conrad Gilliam, Joe Terwilliger, Victoria Haghghi and Jim Russo, of the Columbia Genome Center, René Hen of the Center for Neurobiology and Behavior, and Dr. David Brent of the University of Pittsburgh. Several key genes have been found to be associated with mood disorders, or substance abuse or aggressive/impulsive traits and others with suicidal behavior. A study of the familial transmission of depression, suicidal acts and impulsive-aggressive traits is underway, funded by NIMH grants to Dr. Mann and Dr. Brent (in Pittsburgh).

Neuropharmacology: Dr. Hadassah Tamir and her associates, Kuo-peing Liu and Shu-chi Hsiung, continued to study transduction pathways down stream of 5-HT<sub>1A</sub> receptor and in particular, the cross-talk between the cAMP/PKA pathway and the PI3-K/Akt pathway. They have demonstrated that following activation of 5-HT<sub>1A</sub> receptors with its agonist, in the presence of permeable 8-Br-cAMP, PKA activity inhibited 5-HT-induced formation of the anti-apoptotic agent NFκB. This inhibition is followed by cell death. The mechanism by which PKA induced cell death was shown to involve PKA inhibition of 5-HT-induced IκBα degradation and, as a result, inhibition of nuclear translocation of NFκB. A second mechanism by which 8-Br-cAMP/PKA may cross talk with other transduction pathways was detected. PKA was shown to activate a protein phosphatase (PP2A). PP2A activity down regulates Akt activity and enhances dephosphorylation of Raf<sup>S39</sup> (inhibitory site) thereby up regulates ERK1/2 activity resulting in apoptosis due to diminished activity of NFκB. In addition, enhanced activity of PP2A induced by elevated cAMP/PKA dephosphorylates and activates the pro-apoptotic agent caspase-3. On the other hand, inhibition of PP2A with calyculin A, potentiates Akt activity and attenuates ERK1/2 activity and as a result 5-HT-induced cell survival is enhanced. In summary, our data indicate that 5-HT<sub>1A</sub> receptor is involved in the regulation of multiple intracellular signal transduction pathways. Among these, the regulation of Akt/NFκB activity is crucial for cell viability by coordinating the activities of downstream transcription factors. The activities of PKA/PP2A are essential for homeostasis of this system by regulating NFκB activities at two separate distinct sites. With Dr Arango and the brain bank they have shown deficiencies

in these pathways that may underlie deficiencies in cortical neurons in depression and suicide.

*Serotonin Neurophysiology and MicroPET:* Dr. Mark Underwood conducts research into the regulation of serotonergic neurons in the dorsal raphe nucleus in the postmortem human brainstem in suicide and alcoholism. The studies examine serotonergic neurons directly and define their functional capacity using quantitative morphometric and receptor binding methods. Dr. Underwood and colleagues are also performing translational studies examining gene-environment interactions and effects on the development of the serotonergic system in the brain of transgenic mice and how this affects behaviors in adulthood. He directs the Department of Neuroscience *in vivo* imaging studies in rodents using microPET methods supported by the Radioligand Laboratory of Columbia University. He chairs the Columbia University Medical Center Institutional Animal Care and Use Committee (IACUC).

*Neurophysiology:* Research in the Rayport laboratory focuses on the synaptic underpinnings of schizophrenia and drug dependence. The main research focus is on the actions of dopamine neurons, which Rayport and colleagues have shown use glutamate as a cotransmitter. In transgenic mice with fluorescent dopamine neurons, made in collaboration with René Hen, Nao Chuhma has shown that coreleased dopamine dynamically regulates the glutamatergic signaling of the neurons. In collaboration with David Sulzer and Robert Edwards (Neurology/UCSF), Chuhma has shown that transgenic disruption of glutamatergic pathways reduces dopamine neuron glutamatergic synaptic transmission. Won Yung Choi and Emily Rhodes Lowry are exploring the synaptology of dopamine neurons, asking whether the neurons make separate dopaminergic and glutamatergic synapses. To assess more broadly the role of glutamatergic pathways in schizophrenia, Inna Gaisler-Salomon and Gretchen Mae Miller, in collaboration with Holly Moore, Jay Gingrich and Scott Small (Neurology/Columbia University), are using a third line of transgenic mice with a subtle disruption in glutamatergic synaptic transmission (which were made in collaboration with René Hen), to test the NMDA receptor hypofunction model of schizophrenia. Takeo Mizuno, in collaboration with Claudia Schmauss, is exploring dopamine action in the nucleus accumbens, a principal target of CNS dopamine neurons. Focusing on the intrinsic synapses made by the medium-spiny GABA neurons, which comprise 95% of the neurons in the area, Mizuno is using two-photon microscopy to identify the dopamine receptors involved in the modulation of single accumbens synapses. In a translational focus, Man Jiang, in collaboration with Jonathan Javitch and Marc Laruelle, is asking whether dopamine receptor internalization accounts for altered PET measures of dopamine synaptic function in schizophrenia. Together the goal of these studies is identify neuroplastic mechanisms that may prove to be novel drug targets for the pharmacotherapy of schizophrenia and drug dependence.

*Neurotransmitter Regulation:* Dr. David Sulzer's laboratory is pursuing the modulation of dopamine release at the presynaptic level leading to identification of the precise roles of antipsychotics and amphetamine. In new work they find that the vesicles may mediate exocytosis through extremely fast pore flickering, and demonstrated the first direct evidence that quantal size can be changed in the CNS. In new work, they have elucidated the effects of dopamine release on plasticity of the cortical-striatal synapse that is thought to underlie the reward pathway, drug dependence, and motor control. They have been examining the effects of dopamine oxidation in neurodegeneration, which appears to underlie the neurotoxicity due to methamphetamine, the biosynthesis of neuromelanin, and cellular alterations that could underlie Parkinson's Disease.

*Molecular Recognition:* Dr. Jonathan Javitch's research focuses on understanding the structural bases for the function of G protein-coupled receptors and neurotransmitter transporters. His group has studied the dopamine D2 receptor, the principal site of action of antipsychotic drugs, and the dopamine transporter, the site of action of the psychostimulants cocaine and amphetamine. One focus of the group is the structural basis of receptor and transporter dimerization and its importance in activation or transport. Another research project focuses on bacterial transporters that are related to human neurotransmitter transporters but can be produced in large quantities for direct structural studies. Other studies are devoted to understanding the role of phosphorylation of the amino-terminus of the dopamine transporter in regulating the actions of amphetamine.

Developmental Disorders: Dr. Welch is exploring the biological mechanisms of nurture and testing new treatments for developmental, behavioral disorders and inflammatory disorders. She recently formed a collaboration with Michael Gershon in the Department of Pathology and Cell Biology that is known as the BrainGut Initiative. The Initiative will further investigate mechanisms activated by nurture that condition the brain-gut axis and influence behavior. New studies build on prior collaborative animal research that was done with Dr. David Ruggiero demonstrating for the first time that the gut peptide secretin is synthesized in the forebrain by the hypothalamus and demonstrating that chronic GI inflammation activates brain patterns in areas known to be abnormal in autism. Current research is testing the hypothesis that gastrointestinal inflammation and concomitant brain effects may be effectively treated with combined secretin and oxytocin in acquired and congenital/genetic rodent models of colitis.

Human Genetics and Neurochemistry: Dr. Mann and Yung-yu Huang have been studying CSF monoamine metabolites and other neurotransmitter systems including peptides such as CRF and substance P, GABA and glutamate in collaboration with Tom Cooper in man and non-human primates. Studies investigate genetic and rearing effects on transmitter levels and behavior. With Drs Haghghi, Terwilliger, Gilliam, Russo and Goldman, candidate genes are being studied in postmortem brain tissue and blood or saliva samples from families and unrelated patients and controls to examine genetic and environmental effects on the brain and psychopathology.

### ***Neuropathology***

The Division of Neuropathology conducts basic and clinical research and participates in postgraduate medical education. It provides a neuropathology service to the New York State Office of Mental Hygiene (OMH). The Neuropathology Division examines the brains of OMH patients obtained at autopsy and it maintains an archival collection of these specimens.

Chemical Neuroanatomy and The Diane Goldberg Laboratory for Molecular Imaging of Neural Disorders: Dr. Victoria Arango and her colleagues conduct postmortem studies of suicide victims and alcoholics that utilize a combination of quantitative receptor autoradiography, *in situ* hybridization histochemistry and morphometric analysis of forebrain and brainstem nuclei. Her collaborators are Drs. Mark D. Underwood, Hadassah Tamir, J. John Mann, Helene Bach-Mizrachi, Loubna Erraji-Benchekroun and Maura Boldrini, as well as Suham A. Kassir and Yung-yu Huang. Dr. Arango directs the Brain Bank of the Conte Center for the Neuroscience of Mental Disorders. All cases, now collected in the Republic of Macedonia, undergo a detailed psychological autopsy, a toxicological screen including brain and hair analyses and neuropathological examination. In addition to demonstrating that suicide victims do not have fewer serotonin-synthesizing neurons or processes in the dorsal raphe nucleus, Dr. Arango and colleagues showed an increase in the level of tryptophan hydroxylase (TPH) protein and mRNA in the brainstem of suicide victims.

Using 3-D stereology, they found decreased neuronal density in the orbital, but not in the dorsal prefrontal cortex of suicide victims. They derived a *binding index*, the ratio of receptor binding to neuron density (fmol/mg tissue)/(neurons/mm<sup>3</sup>). 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> binding indices were higher in orbital cortex in the suicide group, but were not different in BA9. These results lend support to a serotonergic abnormality in the ventrolateral prefrontal cortex of the brains of suicide victims, while the dorsolateral prefrontal cortex is largely spared.

Taken together, these studies revealed fundamental neurochemical differences between suicide victims and mood disorder patients. They indicate that morphological differences between controls and suicides are primarily confined to the ventral prefrontal cortex, while the dorsal prefrontal cortex remains largely unaffected. A collaboration with Dr. Lisanby, examines the neuroanatomical effects of electroconvulsive therapy and magnetic seizure therapy in nonhuman primates, including the examination of cell proliferation in the hippocampal formation following these seizure-inducing interventions. Other collaborations of Dr. Arango

include postmortem studies of the cannabinoid 1 receptor with Dr. Vinod Yaragudri and Appa Hungund from the Nathan Kline Institute and molecular biology studies with Charles Glatt from Weill-Cornell. Dr. Arango also collaborates with Dr. Fatema Haghghi on a methylation study in depression and with Dr. Gil Zalsman on a SNP microarray study of depression and suicide. These various projects are supported by NIMH, NIAAA, The Stanley Medical Research Institute, and the American Foundation for Suicide Prevention for postmortem human brain research. The postdoctoral fellows, Dr. Boldrini, Dr. Scalia and Dr. Bach-Mizrachi have all secured AFSP and NARSAD awards. Dr. Boldrini is the recipient of the Janssen Fellowship for Translational Neuroscience.

Neuropathology: Dr. Andrew J. Dwork and colleagues study neuropathological features of schizophrenia and mood disorders, and neuropathological correlates of the dementia that is common among elderly individuals with schizophrenia. Current projects include: (1) Structural abnormalities of dendrites in schizophrenia, mood disorders, and animal models of these illnesses and their treatments. These studies employ our NeoGolgi method of neuronal impregnation, which is the first to provide predictable and uniform Golgi impregnations. Animal studies are conducted in collaboration with Drs. Coplan, Gingrich, Lisanby, Moore, Perera, and Role. (2) Neuropathological correlates of dementia in schizophrenia. These studies are currently focused on white matter pathology. (3) Collection of brains and clinical data from autopsies of psychiatric patients, suicides, and comparison cases in the Republic of Macedonia. Material from this collection is employed in numerous studies within the Department of Neuroscience and in collaboration with other departments and institutions. (4) A historical study using the ecological introduction of neuroleptic drugs to determine the effect of the duration of untreated psychosis on the course of schizophrenia after the initiation of antipsychotic treatment. (This is a NARSAD Young Investigator project by Dr. Branislav Mancevski.) (4) Studies of the role of neurogenesis in the response of animal models of depression to antidepressant treatments. (5) A multi-laboratory collaboration, organized by Dr. Alan Brown, to investigate abnormalities of microtubules in schizophrenia and animal models of schizophrenia.

Molecular Biology and Behavior: Dr. Claudia Schmauss' research program uses molecular, biochemical, and anatomic approaches to study the expression and function of neurotransmitter receptors that are targets for drugs with antipsychotic and antidepressant potencies. One major project in Dr. Schmauss' laboratory focuses on elucidating the roles of two members of the D2-class of dopamine (DA) receptors, named D2 and D3 (the main targets for neuroleptic drugs), in modulating higher cognitive functions. Dr. Schmauss' laboratory has shown that knockout mice lacking DA D2 and D3 receptors have significant impairments in spatial working memory and that D2 receptor inactivation also impairs performance in cognitive tasks requiring sustained attention. These deficits in working memory and/or sustained attention are not only reflected in decreased activation of prefrontal cortical neurons, they also correlate with altered induction of expression of a small group of regulatory transcription factors that normally respond to tasks of higher cognitive functioning. These findings are of importance in view of our increasing awareness that, although neuroleptic drugs blocking D2-like receptors are efficacious in diminishing positive symptoms of schizophrenia, they show little efficacy in ameliorating cognitive the deficits that accompany the disease. Further studies are now underway that explore mechanisms underlying these cognitive malfunctions.

A second major project investigates the posttranscriptional processing of the serotonin (5HT)2C-receptor-encoded pre-mRNA (known as RNA editing) in human prefrontal cortex and mouse forebrain neocortex. These studies identified significant, site-specific alterations in the editing of 5-HT2C pre-mRNA in the prefrontal cortex of depressed suicide victims that result in a predominant expression of 5-HT2C receptor isoforms with decreased sensitivity to 5-HT. Subsequent studies on different inbred strains of mice illustrated how changes in the synaptic concentration of serotonin affects editing-site preferences in 5-HT2C pre-mRNA, and exposure of an spontaneously anxious inbred strain of mice to early life stress revealed changes in 5-HT2C pre-mRNA editing in the adult brain that resemble those detected in subjects with major depression. Current studies that investigate the molecular mechanisms leading to altered 5-HT2C pre-mRNA editing in mice exposed to early

life stress and their modulation by antidepressant drugs and environmental enrichment found altered expression of isoforms of the editing enzymes ADAR1 and ADAR2 that have different catalytic activities and that accompany not only changes in 5-HT<sub>2C</sub> pre-mRNA editing, but also changes in editing of other neuronal genes.

*Molecular Neuroanatomy:* David A. Ruggiero, PhD and colleagues study prenatal and postnatal risk factors, which have been associated with pediatric developmental disorders such as the *sudden infant death syndrome* (SIDS) and autism. Much effort has been directed at developing animal models to identify endogenous and/or exogenous physiological stressors that may evoke pathophysiological activity in autonomic circuits regulating cardiac and other visceral activity patterns. This work dovetails with a collaboration with the Welch Laboratory of Childhood Developmental Disorders investigating the mechanisms underlying brain/gut stress in animal models of inflammation.

### ***Brain Imaging***

Ramin Parsey MD, PhD is the Director of the Brain Imaging Core. Dr. Todd Ogden is the senior brain image analysis statistician and has developed novel innovations in methods and software for kinetic modeling and analysis of PET neuroreceptor binding studies. Dr. Ogden, together with the kinetic modeling expertise of Dr. Ramin Parsey, and the programming skills of Dr. Ashish Ojha, has developed a new voxel-based image analysis routine. Dr. Kjell Erlandsson, a PET physicist, has added valuable expertise in kinetic modeling and signal processing.

The Division is continuing to study unipolar and bipolar depressed subjects before and after treatment with an SSRI or ECT, bipolar depressed subjects, suicide attempters and non-attempters, and healthy volunteers. These studies have generated important new data that for the first time demonstrate that many of our findings in postmortem human brain tissue can be detected in vivo in depressed subjects. Abnormalities detected in currently depressed subjects are now being investigated in remitted depressed subjects in an effort to determine if biological abnormalities are state or trait phenomena. In addition, we are continuing our non-human primate PET studies focusing on new ligand development and evaluation, endogenous competition studies, and blocking studies. We are continuing to improve our ability to study neurotransmitter systems in the microPET camera using rodents and monkeys. That program is funded by the two center grants, and grants awarded to Drs. Mann and Dileep Kumar. Dr Kumar also has received a grant from the NIMH to develop a CFR1 ligand.

Drs. Dileep Kumar, Ted Wang, Jaya Prabhakaran and Vattoly Majo are an outstanding group of organic chemists. As a result of their expertise, we have introduced novel PET tracers for the serotonin transporter and other serotonin receptors into human studies, and we are developing additional novel ligands. We have also filed two patents based on these studies. Collaborations have been developed with several groups in neurology and other P.I. investigators using some of our PET tracers. We have continued our structural brain studies with quantitative MRIs of subjects enrolled in the PET studies and have used a voxel based analytic approach to find alterations in brain structure in mood disorders. Our efforts have been greatly assisted by collaborations with the Department of Radiology (Ronald van Heertum, MD, Joy Hirsch, PhD and Peter Esser, PhD). In collaboration with Dr. De La Paz, Dr. John Keilp has an AFSP grant to study cognitive function with fMRI.

Dr. Gregory Sullivan has expanded the application of the serotonin system PET imaging to particular anxiety disorders. This includes an AFSP-funded study of the relationships between serotonin system functioning and suicidal behaviors in comorbid PTSD and depression, as well as a NARSAD-funded study of serotonin and stress axis interactions in PTSD. Dr. Sullivan is also beginning recruitment for [<sup>15</sup>O]-water and serotonin receptor PET imaging studies of panic disorder, funded by a grant from the Dana Foundation and his K08 career development award.

Dr. Matthew Milak is an Assistant Professor and has been working on the correlations between

neuropsychological and psychological measures and brain glucose metabolism and receptor density. He is now a recipient of two new grants, examining the deficits of the 5-HT<sub>1A</sub> receptor system as a trait marker in healthy offspring of probands with major depressive disorder supported by NARSAD, and a second one studying 5-HT<sub>1A</sub> receptor activation as an index of antidepressant efficacy, supported by the Paul Janssen Young Investigator Award. During 2006 he received an NIMH funded K08 career development award funding the development and characterization of the first agonist 5-HT<sub>1A</sub> radioligand we have shown to successfully label 5-HT<sub>1A</sub> receptors in non-human primates.

We collaborate on NIH funded imaging studies with Dr. Davangere Devanand in Biological Psychiatry, Dr. Evelyn Attia in Eating Disorders, Dr. Richard Sloan in Consultation Liaison Psychiatry, Paul Harris and Rudi Liebel in Diabetes, Yaacov Stern in Neurology. We have funded studies from several companies for occupancy studies with new therapeutic agents and for development of novel PET tracers for new molecular targets.

Ongoing funding from NIMH and foundations include two center grants (Conte Center for the Neuroscience of Mental Disorders and The Stanley Medical Research Institute), NIMH R01 grants, a NIH K01 award, NIMH K08 grants, American Foundation for Suicide Prevention grants, Clinical Trials Office, Dana Foundation and NARSAD grants.

### **Awards/Honors**

Dr. Branislav Mancevski's 2005 NARSAD Young Investigator Award was selected for the NARSAD 2005 Research Partners Program

Dr. Maria A. Oquendo received a Suicide Scholar Award from Eli Lilly in March 2006 for one year

Dr. Gorazd Rosoklija was elected to lifetime membership in the Macedonian Academy of Sciences and Arts

Dr. David Sulzer was awarded a Columbia "ISE" (Integrated Science & Engineering) Award for exploratory research at Columbia University

K awards to Drs. Hanga Galfalvy and Maté Milak.

Conte Translational Neuroscience Center started a second five-year funding period.

New Developing Center in Suicide Prevention funded by NIMH (PI: Barbara Stanley).

### **Publications**

Baca-Garcia, E; Diaz-Sastre, C; García Resa, E; Blasco, H; Braquehais Conesa, D; Oquendo, MA; Saiz-Ruiz, J; de Leon, J. Suicide attempts and impulsivity. *European Archives of Clinical and Psychiatric Neuroscience*. 2005; 255(2):152–156.

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