

Therapeutics

The Department of Therapeutics is comprised of four interactive sub-divisions that conduct research in mood, anxiety and related disorders. As Director of the department, Dr. Donald Klein has provided scientific and administrative guidance on methodology, critical evaluation, and future directions of research for over 30 years. On the occasion of his retirement this year, Dr. Klein's contributions to the development of psychiatry and psychiatric research during his long and productive career were honored at the Donald F. Klein Symposium in October 2006. These reflections featured review of his seminal works and their impact on psychiatry. Although his absence in leadership from the post of Director of Research will be felt, we are delighted that he will become Professor Emeritus and continue his contributions as investigator, mentor, and consultant.

The Depression Evaluation Service

Overview

The Depression Evaluation Service (DES) was begun in 1977 by Dr. Frederick Quitkin, who sadly succumbed to cancer in October 2005. Dr. Quitkin's vision was the study of diagnosis, pathophysiology, and treatment in mood disorders using therapeutic response as a nosologic tool. His legacy includes the development of an evidence base for the diagnosis of "atypical" subtype of mood disorders which resulted in its being included in DSM-IV as a validated sub-type. Other major studies conducted under his direction have included: prediction of relapse after successful treatment with serotonin reuptake inhibitor antidepressant medication, treatment of depression which co-occurs with alcohol or drug dependence, innovative treatment of explosive mood disorder in adolescents, genetic predictors of antidepressant medication response, and brain imaging to subtype depressive disorders. The DES has participated in the design of a major NIMH clinical trial entitled "Sequenced Treatment Alternatives to Relieve Depression" (STAR*D) and has been one of the Regional Centers in that recently completed landmark study.

Patrick J. McGrath, MD, Co-Director, Depression Evaluation Service, Professor of Clinical Psychiatry

Jonathan W. Stewart, MD, Co-Director, Depression Evaluation Service, Professor of Clinical Psychiatry

Edward V. Nunes Jr., MD, Professor of Clinical Psychiatry

Deborah Deliyannides, MD, Assistant Clinical Professor of Psychiatry

Stephen Donovan, MD, Assistant Professor of Clinical Psychiatry

David Hellerstein, MD, Associate Professor of Clinical Psychiatry

Vito Agosti, C.S.W., Research Scientist, Senior Staff Associate

Sarai Batchelder, PhD., Research Project Manager III

Donna O'Shea, MsEd, Clinical Researcher Level III

Carmen Prieto, Senior Lab Technician

Current Research

The large NIMH effectiveness trial of the treatment of Major Depression (Sequenced Treatment Alternatives to Relieve Depression – STAR*D) was completed with Dr. Patrick J. McGrath taking over as Regional Center Director for New York, resulting in multiple high-profile publications. This study is the first to test in a randomized trial of adequate power the effectiveness of standard treatment strategies for patients who are unresponsive to a first SSRI trial for Major Depression. Data collection was also completed for Dr. McGrath's STAR*D Alcohol Study, an ancillary study funded by the National Institute on Alcohol Abuse and Alcoholism, comparing the response rate to antidepressant for persons with concurrent alcohol use disorders and depression to those with uncomplicated depression. Another of Dr. McGrath's initiatives involved whole genome association genotyping of 1,900 subjects from STAR*D. This was completed in a collaborative effort with Dr. Hamilton at the University of California, San Francisco, resulting in important new findings regarding the genetic predictors of antidepressant response.

Dr. Jonathan Stewart has completed pilot data collection to assess the efficacy of several sequential treatments for patients with refractory depression. This cross-over assignment design compared the efficacy of tranylcypromine, tranylcypromine plus dextroamphetamine, and tranylcypromine plus triiodothyronine in the remission of treatment resistant depression. Dr. Stewart has also received a new grant from Eli Lilly and Company to pilot the effectiveness of duloxetine in the treatment of Major Depressive Disorder and Dysthymia with Atypical features. Ongoing collaborative neuropsychological studies explore the correlates of f-MRI testing among other measures of brain functioning, seek to determine whether f-MRI findings demonstrate specific brain areas which differ between responders and non-responders to SSRI treatment, and investigate whether hemispheric laterality preferences in auditory processing are correlated with treatment outcome among 3 treatment groups, including placebo, fluoxetine, and imipramine.

Dr. Stephen Donovan continues his work on the relationship between aggression, particularly non-predatory aggression and substance abuse risk with the publication of two book chapters on this subject, one for psychiatric clinicians and one for substance abuse counselors. He continues work on the pharmacological treatment of different types of non-predatory aggression in the tradition of pharmacological dissection developed by Dr. Donald Klein. He has completed a National Institute of Drug Abuse (NIDA) funded study of divalproex-responsive aggression and marijuana use. In collaboration with NIDA's Clinical Trials Network, Phoenix House, Odyssey House and industry support, he plans a proof of concept study demonstrating one can study pharmacologic prevention of substance abuse in high risk aggressive adolescents by using their similar substance dependent older siblings as case markers when they are referred to one of the above substance abuse treatment programs.

The Depression Evaluation Service has recently welcomed the addition of Dr. David Hellerstein to the department. Dr Hellerstein has five ongoing psychopharmacology studies at the Mood Disorders Research Program located at Roosevelt Hospital, where colleagues also include Dr. Steven Hyler. These studies are mostly involved with

treatment of dysthymia, but also include augmentation of treatment-resistant depression, and treatment of SSRI-induced sexual dysfunction. To the DES he brings an efficacy study entitled "Duloxetine for chronic depression: a double-blind study" which also includes multi-faceted MRI imaging: anatomical, functional, MR spectroscopy and diffusion tensor imaging. This work will be supplemented by a new grant from Eli Lilly and Company.

Highlights

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) and its ancillary studies were completed and have generated many contributions to the psychiatric literature.

Drs. McGrath and Stewart assumed Co-Directorship of the Depression Evaluation Service in November 2005.

The Donald F. Klein Symposium, an all-day celebration of the contributions to psychiatry of Donald F. Klein, MD, featuring presentations of his seminal works and their impact on psychiatry was held in October 2006.

The Department welcomed David Hellerstein, MD, an expert in the assessment and treatment of dysthymia and his Project Coordinator, Sarai Batchelder, PhD to the department in July 2006.

HIV Clinical Research Program

Judith Rabkin, PhD, MPH, Professor of Clinical Psychology in Psychiatry

Richard Rabkin, MD, Instructor in Psychiatry

Martin McElhiney, PhD, Research Scientist II

Manuel de la Nues, Research Assistant

Overview

The HIV Clinical Research Program, in operation since 1989, has been conducting clinical trials with HIV+ patients to treat conditions ranging from major depression and dysthymia to hypogonadism and associated symptoms, wasting and fatigue.

Current Research

Currently active studies include an NIH funded randomized placebo controlled trial of modafinil for the treatment of clinically significant fatigue in HIV+ patients taking antiretroviral medication. This grant was awarded in 2005. We also completed data collection in a longitudinal study of terminally ill patients with AIDS or cancer and a non-paid caregiver, to evaluate mood status (depression and positive mood) as death approaches, as well as related issues.

Several pilot studies are underway. The first, funded through the Substance Use Research Center's pilot study program, is designed to determine whether modafinil in combination

with motivational interviewing/cognitive behavioral therapy for 4 months is effective in treating crystal methamphetamine abuse in HIV+ gay men. To date 12 patients have been treated.

Another ongoing pilot study is an open label trial of modafinil to treat fatigue in patients with amyotrophic lateral sclerosis (ALS), in collaboration with the ALS/MDA Center and Drs. Paul Gordon and Hiroshi Mitsumoto, in the Department of Neurology. We are also co-investigators in a longitudinal study being designed by Dr. Gordon to evaluate cognitive function and changes in ALS patients, including interviews with family caregivers.

Finally, we are continuing a double blind randomized trial of DHEA for non-major depression in order to assess neuropsychological test performance before and after treatment. This large NIMH-funded study was originally intended for the treatment of non-major depression. We enrolled 145 HIV+ patients and published the findings in the January 2006 issues of the Am J Psychiatry. The neuropsychological component was added later and so we are still conducting the trial to obtain an adequate sample to determine whether DHEA, which is a neurosteroid, has positive effects on neurocognitive functioning.

Awards/Honors

Dr. David Hellerstein: 2005 Gary M. Spero Memorial Grand Rounds Lecturer, Department of Psychiatry, New York Hospital

Drs. Patrick J. McGrath and Jonathan W. Stewart: Grand Rounds Lecturers at the New York State Psychiatric Institute and the Department of Psychiatry of the Columbia University College of Physicians and Surgeons.

Publications

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Anxiety Disorders Clinic

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Donna Vermes, M.S., N.P.P., Administrator, Psychiatric Nurse 11

Lawrence Amsel, MD, Assistant Professor of Clinical

Ivan Balan, PhD, Research Project Manager 111

Carlos Blanco, M.D, PhD, Psychiatrist 11

Tatyana, Biyanova, PhD., Senior Research Worker

Raphael Campeas, MD, Research Psychiatrist 11

Joan Cook, PhD, Assistant Professor of Clinical Psychology (in Psychiatry)

Christine Fernandez PhD., Research Scientist 11

Elizabeth Jackson, MD, Research Interviewer

Ronit Kishon, PhD., Senior Research Worker

Roberto Lewis-Fernandez, MD, Psychiatrist 11

Michael, Maher, PhD., Research Scientist 11
Randall Marshall, MD, Research Psychiatrist 111
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Sapana Patel, PhD, Postdoctoral Research Fellow
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Franklin Schneier, MD, Research Psychiatrist 11
Smit Sinha, MD, Assistant Clinical Physician 111
Eun Jung Suh, PhD, Research Scientist 11

Overview

The Anxiety Disorders Clinic (ADC) at NYSPI was established in 1982 to study the diagnosis, pathophysiology, and treatment of anxiety disorders. The clinic has grown over the years and now includes programs in social anxiety disorder, obsessive-compulsive disorder, posttraumatic stress disorder and related traumatic conditions (Division of Trauma Services), generalized anxiety disorder, anxiety and depression in Hispanic Americans (Hispanic Treatment Program), pathological gambling, anxiety and depression in patients seen in primary care and other medical specialties. Studies include effectiveness trials in community settings, efficacy trials in specialty clinics, and brain imaging studies investigating pathophysiology. We are examining pharmacotherapy, psychotherapy (cognitive-behavioral therapy, interpersonal therapy, motivational interviewing), and complementary medicine approaches. We are also conducting epidemiological and services research. Our mission is to improve the outcome of our patients by the development and study of new therapeutic strategies, the dissemination of evidence-based practices to clinicians and patients, and the elucidation of the brain mechanisms underlying their symptoms.

Current Research

OCD program: Drs. Liebowitz and Simpson completed their multi-site R01 that examined the efficacy of CBT augmentation of SRI pharmacotherapy in OCD. Dr. Simpson received NARSAD funding to adapt Motivational Interviewing (MI) to improve treatment adherence in OCD. She subsequently received NIMH funding (R34) to further develop her MI intervention and to test it in a randomized controlled trial.

Anxiety, Medical Illness and Addictions: Dr. Blanco obtained funding from NYS Office of Alcoholism and Substance Abuse Services (OASAS) to expand his pathological treatment program and add a new prevention program. In collaboration with Dr. Grann (Herbert Irving Comprehensive Cancer Center) he also started a study to treat with interpersonal psychotherapy (IPT) depressed women with breast cancer.

Generalized Anxiety Disorder: Drs. Schneier and Belzer obtained industry funding to study treatment with cognitive-behavioral therapy and escitalopram, and began collaborating with Dr. Joy Hirsch of CUMC to study brain circuits mediating emotion processing in GAD.

Social Anxiety Disorder: Dr. Liebowitz continued a multi-site study of cognitive-behavioral therapy and paroxetine. Dr. Schneier continued a collaboration with Dr. Gorenstein (Surgery) to study social anxiety in hyperhidrosis patients.

Division of Trauma Studies and Services: Dr. Marshall began a pilot project to develop a manualized group intervention to increase resilience in persons living in lower Manhattan and affected by the 9/11 attacks, funded by the Red Cross. Tatyana Biyanova and Marshall developed the first empirically derived assessment scale that captures cognitive domains of human appraisal of traumatic events. On ongoing RO1 is examining treatment of persons with 9/11-related PTSD, comparing Exposure therapy + paroxetine CR to exposure therapy + placebo. Dr. Neria obtained funding from the SPUNK fund to conduct a clinical trial in patients suffered from 9/11 complicated grief.

The Hispanic Treatment Program continued to conduct a) an R34 from NIMH on a novel approach based on the DSM-IV Cultural Formulation to help bridge the care of depressed Hispanic patients from primary care to specialty mental health services, and b) a project funded by the American Red Cross to provide medication and psychotherapy services to Hispanics still suffering from anxiety and depressive disorders as a result of 9/11. We also have an R01 application under review to test an intervention based on motivational interviewing to improve retention and treatment outcome in depressed Hispanics on antidepressant therapy.

Educating and Training

Kenneth Belzer continued a research fellowship focused on integrative treatment of generalized anxiety disorder. Sapana Patel, another research fellow, obtained a Frontier Fund award to conduct a pilot study of mindfulness meditation therapy for anxiety disorders and is working on a K23 application to the NIMH Services Committee. Smit Sinha completed the 3rd year of his K award under the mentorship of Dr. Don Klein. Dr. Joan Cook completed an NIMH R21 in May 2006 on patient and physician factors that influence chronic benzodiazepine use. She also just completed the first year of her NIMH K01 career development award examining psychotherapy dissemination to front-line clinicians, and the second year as a co-principal investigator on a VA grant examining the efficacy of a new psychotherapy for combat-related nightmares at the Philadelphia VA Medical Center/University of Pennsylvania. As a group, we also participate actively in the teaching and supervision of PGY-2, PGY-3, and PGY-4 psychiatric residents, organizing and running several core classes (e.g., Anxiety Disorders Class for PGY-2 residents) and providing lectures (e.g., psychopharmacology of anxiety disorders, cognitive-behavioral therapy of anxiety disorders) in other core classes. Drs. Simpson, Marshall, and Schneier also delivered lectures for the Departmental Annual Review of Psychiatry.

Clinical Activities

We conduct clinical research in the Anxiety Disorders Clinic.

Awards/Honors

Dr. Lewis-Fernandez was named to the Selection Committee for the Welcome Back Awards, a national program sponsored by Eli Lilly and Company, which has recognized courage and achievement in the mental health community for the last 8 years. He was also named to the NIMH Review Group, Mental Health Services in MH Specialty Settings. He was also named to the APA Committee on Psychiatric Diagnosis and Assessment, which participates in the planning for DSM-V.

Dr. Simpson was nominated to the Scientific Advisory Board of the Anxiety Disorders Association of America. She was also appointed to the American Psychiatric Association's Workgroup to develop practice guidelines for OCD (to be published Fall 2007 in the American Journal of Psychiatry).

Dr. Marshall was appointed Advisor to a new philanthropy devoted to mental health after disaster: Psychiatrists, Psychologists, and Social Workers with Borders, and elected to Best Doctors in America.

Grants

Dr. Simpson received the NARSAD Young Investigator Award (7/05), 1 R34 (3/06), and 2 R01s (9/06).

Dr. Blanco received award of 2 R01s (9/06)

Dr. Lewis-Fernandez was awarded a contract from the NYC Division of Mental Hygiene to evaluate the City's program to promote the diagnosis and treatment of depression in primary care.

Dr. Marshall received a grant from the Red Cross titled "Promoting Adaptation and Resilience in New Yorkers Directly Affected by 9/11: An Intensive Coping Skills Enhancement Group Program" (R. Marshall Principal Investigator, with Y Neria and J Cook, Co-Investigator)

Publications

Y. Neria, R. Gross, R. Marshall (Eds.) 9/11: Mental Health in the Wake of Terrorist Attacks. Cambridge University Press. 2006

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Anxiety Genetics Unit

Abby J. Fyer, MD, Director, Research Psychiatrist II

Josh Lipsitz, PhD, Associate Professor of Clinical Psychology in Psychiatry,

Assistant Professor of Clinical Psychology in Psychiatry

Lindsey Nederlander, PhD, Research Associate

Matthew Malter-Cohen, MS, Research Associate

Overview

Our main goal is to understand genetic contributions to human anxiety and anxiety disorders. We are involved in both traditional family/linkage studies, and neurobiologically based “endophenotypic” and “translational” studies. Current family/linkage study projects include participation in a collaborative linkage study of panic disorder, a pilot study to assess the potential of an isolate population for genetic study of panic, and continued analysis of our large anxiety disorder family study data base to investigate possible familial subtypes of anxiety disorders. The focus of our endophenotype/ translational work is on psychophysiological based paradigms involving associative learning of fear and safety.

Drs. Fyer and co-investigator Dr. Lipsitz also have a background in clinical and diagnostic studies of anxiety and continue to work in these areas. Dr. Lipsitz’ main interest is the psychiatric implications of unexplained somatic symptoms in youngsters and the development of interventions to alleviate distress in this population He has also conducted several studies extending use of interpersonal psychotherapy to anxiety disorders.

Current Research

During the past year Dr. Fyer’s group has continued collection of psychophysiological data and DNA samples for our genetic study of fear conditioning. These samples have been genotyped on a series of candidate genes derived from homology to murine genes known to be involved in either innate fear or fear learning behavior. Analysis of this data including development of psychophysiological defined phenotypes is now underway. In collaboration with Dr. Joy Hirsch, we are conducting pilot study to further evaluate our genetic study subjects using fMRI paradigms that explore the interaction between cortical and sub-cortical neural circuitry involved in response to frightening stimuli. We have also completed collection of an isolate population pilot sample of panic disorder triads and are beginning a pilot genetic and psychophysiology study of safety training in collaboration with Dr. Michael Rogan (Neurobiology and Behavior).

Dr. Lipsitz continues to study applications of interpersonal psychotherapy for anxiety disorders with trials completed for social anxiety disorder and panic disorder. He has expanded his research to the study of somatic complaints in children and adolescents. He is now completing an NIMH-funded study of anxiety disorders and other psychological features of youngsters with unexplained chest pain who are evaluated by a pediatric cardiologist. Dr. Lipsitz has expanded this work to the pediatric emergency department.

Together with Dr. Merav Gur, he has developed a psychosocial intervention to alleviate pain and distress in youngsters with persistent chest pain.

Education and Training

Dr. Fyer is included in the preceptor staff of two training grants: Genetics of Complex Disorders (Dr. Sue Hodge) and Research Training in Affective and Related Disorders (Dr. Ron Rieder). Her most recent fellow (Dr. Yajuan Choy) completed the latter training program in July 2006. Dr. Fyer is also the Department of Psychiatry coordinator for the office of the Associate Dean for Gender Equity and Career Development.

Awards/Honors

Dr. Merav Gur obtained an award from the Advanced Center for Intervention and Services Research (ACISR) of the department of Child Psychiatry to pilot this intervention.

Highlights

Dr. Joshua Lipsitz completed a three-year case-control study of youngsters with unexplained chest pain seen by cardiology specialists.

Dr. Merav Gur obtained a pilot award from the Advanced Center for Intervention and Services Research (ACISR) of the department of Child Psychiatry to pilot a psychosocial intervention for youngsters with unexplained chest pain.

Dr. Lipsitz published results of an open trial of interpersonal psychotherapy for panic disorder.

Dr. Fyer, in collaboration with Drs. Myrna Weissman and colleagues in the Columbia Collaborative Panic Disorder (PD) Genetic Study, published results of their third pass genome scan of PD.