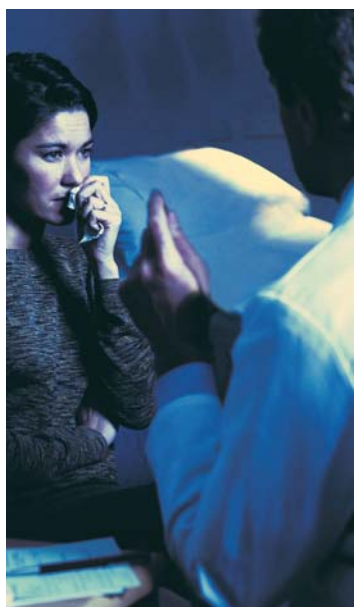


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Borderline Personality Disorder: Researchers Advocate Transference-Focused Therapy



The hallmark symptoms of borderline personality disorder (BPD)—including impulsiveness, emotional dysregulation, and difficulty assessing a clear picture of self and others—can wreak havoc in the lives of patients and their friends and families. After decades of pioneering work on BPD, researchers at Weill Cornell Medical College are continuing to expand the understanding of this disease and are helping to find more effective treatment options.

Otto F. Kernberg, MD, who in the 1960s was the first to name BPD as part of the broader category of severe personality disorders called Borderline Personality Organization, still finds the disease challenging. “The treatment has been difficult and puzzling because they respond only partially to all sorts of available medications,” he explained. “The central therapy is psychotherapy, but of what sort and how should it be constructed?”

To answer this question, Dr. Kernberg and John F. Clarkin, PhD, conducted a yearlong, multiwave study (*Am J Psychiatry* 2007;164:922-928) of 90 patients to evaluate 3 treatments for BPD: dialectal behavior therapy (DBT), a dynamic supportive treatment, and transference-focused psychotherapy (TFP).

DBT, currently the most common therapy for BPD, combines validation of the emotions and experiences of patients with skills training. Supportive treatment is based on psychodynamic principles but is mostly geared to strengthening the patient’s functioning. TFP, an approach developed by the Weill Cornell group, employs a focus on the patient–therapist relationship to interpret the internalized relationships that have significance from the patient’s early years of

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life. It involves patients repeating unresolved relationships from the past with their therapist. Patients also received medications indicated for affective disturbances.

The study was one of the first to look simultaneously at so many carefully defined treatments and is unusual in that it included both men and women. To more closely mirror a real-world scenario, exclusion criteria mimicked those common in clinical practice and patients were assigned to treatment by colleagues in the community.

Although all 3 treatments were effective in reducing anxiety and depression, only DBT and TFP helped reduce suicidal tendencies. TFP was most effective in lessening aggressive impulses. “In addition, we found that only TFP produced an increase in reflective function, which is the capacity to appropriately assess mental states in themselves and other people,” said Dr. Kernberg. “We believe this is an essential function that allows patients to function more deeply in their social lives, work, and intimate relationships.”

Dr. Clarkin also noted that TFP brings unique advantages to treating patients with BPD. “We think that through the therapist’s relationship with the borderline patient in TFP, the patient achieves a more organized and complex sense of self as relating to other people,” he said. He pointed out that, although TFP had the greatest breadth of effect, the study’s optimistic message was that each of the therapy types resulted in clinical changes across various pathology domains. The researchers are now analyzing the data to determine which aspects of personality will predict whether an individual patient with BPD will succeed on a particular therapy. Another paper, currently in press in the

“Through the therapist’s relationship with the borderline patient in TFP, the patient achieves a more organized and complex sense of self as relating to other people.”

—John F. Clarkin, PhD

American Journal of Psychiatry, assesses how a subset of the patients with BPD in the aforementioned study compare to control subjects in their ability to handle negative affect. The researchers collaborated with David Silbersweig, MD, Co-Director of the Functional Neuroimaging Laboratory at New York-Presbyterian/Weill Cornell Medical Center, to assess with functional magnetic resonance imaging (fMRI) the ability of patients to manage negative affect. They found that the 2 groups displayed a significant difference both in behavior and brain functioning level when faced with negative affect. In particular, brain imaging captured differences in organization of the brain between the amygdala and the orbital prefrontal cortex.

If additional funding becomes available, the scientists hope to follow up with further fMRI research. “We’d like to investigate the treatment of borderline patients with TFP to see how it makes effects not only at symptom levels but also at the level of the brain,” said Dr. Clarkin. “Does the brain organization begin to change and to look more like normal people who can handle negative affect?”

John F. Clarkin, PhD, is Attending Psychologist at New York-Presbyterian Hospital/Weill Cornell Medical Center, and is Professor of Clinical Psychology in Psychiatry at Weill Cornell Medical College. E-mail: jclarkin@med.cornell.edu.

Otto F. Kernberg, MD, is Director, Personality Disorders Institute at New York-Presbyterian Hospital/Weill Cornell Medical Center (Westchester Division), Professor of Psychiatry at Weill Cornell Medical College, and is Training and Supervising Analyst, Center for Psychoanalytic Training and Research at Columbia University. E-mail: okernber@med.cornell.edu.

Table. Predicting Change Across 3 Treatments in Patients With Borderline Personality Disorder

	Rate of Change		
	Fixed-Effect Coefficient	P-value	Effect size (r)
Suicidality			
Transference-focused psychotherapy (TFP)	-0.05	0.01	0.33
Dialectal behavior therapy (DBT)	-0.09	0.01	0.34
Supportive treatment	-0.03	NS	0.18
Anger			
Transference-focused psychotherapy	-0.06	0.001	0.44
Dialectal behavior therapy	-0.03	NS	0.25
Supportive treatment	-0.03	0.05	0.28

Source: Clarkin JF et al. *Am J Psych* 2007;164:922-928.

NS, not significant

New Books by Prominent Thought Leaders Shed Light on Psychiatric Disorders

Researchers and clinicians at NewYork-Presbyterian Hospital have been busy writing and editing books that enhance our understanding of psychiatry. The books featured here cover a broad range of topics from developmental and social psychology to treatments for schizophrenia, depression, and eating disorders. For more information on the authors and their work, please visit www.nypppsychiatry.org.



Paul S. Appelbaum, MD

Paul S. Appelbaum, MD, Elizabeth K. Dollard Professor of Psychiatry, Medicine,

and Law at Columbia University, has authored a new book, *Clinical Handbook of Psychiatry and the Law, 4th Ed.* (Lippincott Williams & Wilkins, 2007).

Co-edited by Dr. Appelbaum, the book serves as a guide for mental health professionals, providing useful information on the ways that law affects their practices. The handbook covers a wide range of relevant topics, from malpractice and liability issues to new federal laws protecting patients' privacy and regulating the use of seclusion and restraint. Each chapter is complete with case examples of legal dilemmas, attempting to identify and explain the rationale behind current legislation and also provide a concrete guide to medical action.

Dr. Appelbaum is the author of several books on ethical and legal concerns in the field of medicine; 4 of his books were awarded the Manfred S.

Guttmacher Award. In addition to his professorships at Columbia University, Dr. Appelbaum has served as the President of the American Psychiatric Association and the American Academy of Psychiatry and Law, and is now a member of the MacArthur Foundation Network on Mandatory Outpatient Treatment.



Betty Jo Casey, PhD

The recent publication of *Developmental Psychobiology, Review of*

Psychiatry Series, Volume 23 (American Psychiatric Publishing, Inc., 2004), marks yet another accomplishment for B.J. Casey, PhD, Sackler Professor of Developmental Psychobiology and Director of the Sackler Institute for Psychobiology of Development at Weill Cornell Medical College.

Developmental Psychobiology, edited by Dr. Casey, is a collection of works on brain development and neurodevelopmental disorders. It examines the important issue of brain plasticity in development, and outlines normal behavioral and neural development in an attempt to better target the causes and potential treatments of disorders like Tourette's syndrome and schizophrenia. Finally, Dr. Casey's volume covers a number of new, noninvasive technologies available for investigating neural development.

Dr. Casey, whose areas of study include attention-deficit hyperactivity disorder, obsessive-compulsive disorder, and childhood-onset schizophrenia, is

internationally known for her use of novel and noninvasive neuroimaging methodologies to analyze brain development related to attention regulation. She is a member of numerous advisory boards and the editor of several books and journals. Her work has been featured in *Nature* and by the National Institutes of Health.



Stephen J. Ferrando, MD

Stephen J. Ferrando, MD, Professor of Clinical Psychiatry and Public Health and Vice

Chair for Psychosomatic Medicine, NewYork-Presbyterian Hospital/Weill Cornell Medical Center, has served as senior editor of the annual *Psychiatry-in-Review*, a multimedia board review guide for individuals seeking certification in psychiatry.

The 70-chapter *Psychiatry-in-Review* is a collaborative effort: Written by more than 40 doctors, its authors all hail from the residents and faculty of the NewYork-Presbyterian/Weill Cornell Payne Whitney Clinic. The comprehensive book serves as a thorough and easy-to-use study guide, covering all the essential topics and complete with a drug-interaction study tool and online practice exam.

After medical school, Dr. Ferrando accepted an HIV/AIDS research fellowship funded by the National Institutes of Mental Health at NewYork-Presbyterian/Weill Cornell. Much of his clinical neuropsychiatric research now focuses on quality-of-life aspects of chronic diseases. Dr. Ferrando is

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President of the New York Area Society for Liaison Psychiatry and a 10-year member of the American Psychiatric Association Committee on AIDS, part of the HIV/AIDS treatment guidelines workgroup.



Beatrice A. Hamburg, MD, and David A. Hamburg, MD

Beatrice A. Hamburg, MD, and David A. Hamburg, MD, DeWitt Wallace Distinguished Scholars in the Department of



Psychiatry at Weill Cornell Medical College, recently co-authored the book, *Learning to Live Together: Preventing Hatred and Violence in Child and Adolescent Development* (Oxford University Press, 2004). The Hamburgs are both distinguished in their field. Dr. Beatrice Hamburg has held professorships at Mount Sinai School of Medicine, Stanford University School of Medicine, and Harvard Medical School. She currently serves as a member of the New York City Board of Health and is a member of the American Academy of Child and Adolescent Psychiatry. Her husband, Dr. David Hamburg, is similarly accomplished. He too has held professorships at Stanford and Harvard, and is now a member of the Council of Foreign Relations. He was a member of President Bill Clinton's Committee of Advisors on Science and Technology, and has received such honors as the Presidential Medal of Freedom and the National Academy of Sciences Public Welfare Medal. Both Drs. Beatrice and David Hamburg, along with their daughter Margaret Hamburg, MD, are members of the Institute on Medicine

(IOM), making theirs the only family to ever have three members elected to the IOM.

In their latest book, *Learning to Live Together*, the Hamburgs discuss the harmful teaching of violence, prejudice, ethnocentrism, and other hateful outlooks to children in our society. The book delves into the fields of developmental and social psychology to explore the many psychological aspects of prejudice and the educational steps that may be taken to reduce hatred, in hopes of fostering a less violent and more compassionate course of childhood development.



Jeffrey Lieberman, MD

Jeffrey A. Lieberman, MD, the Lawrence E. Kolb Professor and Chairman of

Psychiatry at Columbia University College of Physicians and Surgeons and Director of the New York State Psychiatric Institute, recently edited his ninth book, *Textbook of Schizophrenia* (American Psychiatric Publishing, Inc., 2006). Schizophrenia is one of the leading causes of disability and premature death among patients with medical disorders, according to the World Health Organization. Dr. Lieberman's latest work stands as a comprehensive examination of the many complex biological mechanisms underlying this debilitating disorder and the various clinical measures available for its management. *Textbook of Schizophrenia* reviews a wide array of information, covering both genetic and environmental risk factors for schizophrenia, and introduces readers to the range of treatment options on hand for the different phases of the disorder. Accessible and thorough, the textbook allows readers to gain a more specific knowledge of

schizophrenia and a better understanding of psychiatry as a whole. As part of his ongoing effort to study the pharmacology and treatment of schizophrenia, Dr. Lieberman currently serves as Principal Investigator of the Clinical Antipsychotic Trials of Intervention Effectiveness Research Program (CATIE) sponsored by the National Institutes of Mental Health. Winner of many awards and honors throughout his career, he is also a member of the National Academy of Sciences Institute of Medicine and the current chair of the American Psychiatric Association Council of Research.



Eric Kandel, MD

Nobel Laureate and Columbia University Professor Eric Kandel, MD, recently

authored a new book, *In Search of Memory: The Emergence of a New Science of Mind* (W.W. Norton, 2006). Dr. Kandel, a graduate of Harvard University and New York University, has spent years studying the molecular basis of memory storage, primarily focusing his research on mice and the marine mollusk *Aplysia*. His latest book is a history of scientific breakthroughs in the study of the mind throughout the past 50 years, interwoven with a personal account of his own life and career, beginning with his earliest experiences in Vienna. Dr. Kandel traces the evolution of his initial interest in history and psychoanalysis into his current fascination with the cellular and molecular mechanisms that underlie memory. In addition to his 2000 Nobel Prize in Physiology or Medicine, Dr. Kandel has been the recipient of numerous honors, including the National Medal of Science U.S.A. and membership in

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the U.S. National Academy of Sciences. He has also won great acclaim for his previous published works, such as the books *Principles of Neural Science* and *Psychiatry, Psychoanalysis and the New Biology of Mind*.



Otto F. Kernberg, MD, FAPA

Otto F. Kernberg, MD, FAPA, recently edited a new textbook entitled *Handbook of Dynamic Psychotherapy for Higher Level Personality Pathology* (American Psychiatric Publishing, Inc., 2007). Dr. Kernberg's book explains the essentials of psychodynamic treatment of personality pathology for higher-level personality disorders; treatment of severe personality pathology is described in a companion volume, *Psychotherapy for Borderline Personality: Focusing on Object Relations*. The handbook serves as a comprehensive guide for clinicians learning the principles of dynamic therapy, outlining goals, strategies, and treatment techniques for long-term treatment of personality pathology.

Dr. Kernberg, Professor of Psychiatry at Weill Cornell Medical College and Director of the Personality Disorders Institute at New York-Presbyterian Hospital/Weill Cornell Medical Center, Westchester Division, has previously authored 12 books and co-authored 11 others. Dr. Kernberg is also the former President of the International Psychoanalytic Association, and winner of numerous awards, including the 1993 Presidential Award for Leadership in Psychiatry from the National Association of Psychiatric Health Systems.



Sarah Hollingsworth Lisanby, MD

Sarah Hollingsworth Lisanby, MD, Associate Professor of

Clinical Psychiatry at Columbia University College of Physicians and Surgeons, has edited 2 new texts, *Brain Stimulation in Psychiatric Treatment: Review of Psychiatry, Volume 23* (American Psychiatric Publishing, Inc., 2004), and *The Oxford Handbook of Transcranial Stimulation* (in press).

The first book offers a look into the developing field of electrical brain stimulation as treatment for neuropsychiatric disorders, examining such methods as transcranial magnetic stimulation (TMS), magnetic seizure therapy (MST), deep brain stimulation, and vagus nerve stimulation. Dr. Lisanby's second book, *The Oxford Handbook of Transcranial Stimulation*, focuses more closely on TMS and its potential applications in the areas of perception, emotion, cognition, and neurophysiology. Both books are meant to serve as tools for students, researchers, and clinicians. Dr. Lisanby is internationally known for her novel adaptation of TMS to perform MST. Her research team is now attempting to develop MST as an alternative to electroconvulsive therapy in the treatment of depression. Dr. Lisanby is the Director of the new Brain Stimulation Service at New York-Presbyterian Hospital/Columbia University Medical Center, a clinical program specifically geared toward the use of brain stimulation for the relief of treatment-resistant depression.

She has authored or co-authored more than 150 published works, has received more than 35 honors and awards, and is a member of the American College of Neuropsychopharmacology.



George J. Makari, MD

George J. Makari, MD, Associate Professor of Psychiatry and Director of the

Institute for the History of Psychiatry at Columbia University, is the author of a new book, *Revolution in Mind: The Creation of Psychoanalysis* (Psychoanalytic Electronic Publishing, 2003).

In his latest publication, Dr. Makari carefully traces the development of psychoanalytic thought, beginning his exploration in the mid-19th century, a period that saw the emergence of clinical psychiatry, neuroscience, academic psychology, and a growing cultural interest in sexuality. Dr. Makari examines all of these factors as important influences on Sigmund Freud, and then continues his study with an investigation of Freud's disciples, following Freudianism from its humble beginnings in Vienna into a widespread international movement.

Revolution in Mind also outlines the evolution of psychoanalysis throughout the 20th century. Far from being a mere biography of Freud, Dr. Makari's interdisciplinary *Revolution of Mind* is a rich synthesis of material, an authoritative intellectual history that should appeal to both mental health professionals and the general public.

In addition to his interests in the history of psychoanalysis, Dr. Makari researches the psychotherapeutic process and linguistics, and is involved in private practice. He has been a member of the Columbia University community for the past 10 years.

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Moira Ann Rynn, MD

Moira Ann Rynn, MD, Associate Professor of Clinical Psychiatry at the

New York State Psychiatric Institute/ Columbia University College of Physicians and Surgeons, contributed a chapter to a new volume on child psychology, *Clinical Manual of Child and Adolescent Psychopharmacology* (American Psychiatric Publishing, Inc., 2007).

Written by a number of renowned medical authorities, *Clinical Manual of Child and Adolescent*

Psychopharmacology is intended both as a detailed guide for practitioners and as an instructive tool for introductory courses in pediatric psychopharmacology. The book first explains the reasons children and teens may not react to psychopharmacological treatment the same way as adults do, and then discusses specific disorders like attention-deficit hyperactivity disorder and bipolar disorder. Dr. Rynn's chapter features anxiety disorders; she weighs both the benefits and risks of various drug therapies in the treatment of anxiety disorders, which often go undiagnosed in the pediatric population.

Dr. Rynn presently serves as the Director of the Children's Day Unit and the Child and Adolescent Psychiatric Evaluation Service at the New York State Psychiatric Institute/ Columbia University College of Physicians and Surgeons. She has extensively studied the use of sertraline as treatment for children with anxiety disorders, and serves as the Chair of the Pharmacotherapy Committee for an National Institutes of Mental Health-funded "Child/ Adolescent Anxiety Multimodal Treatment Study" trial.



Rosemary Stevens, PhD, MPH

A new book, *The Public-Private Health Care State: Essays on*

the History of American Health Care Policy (Transaction Publishers, 2007), was recently authored by Rosemary Stevens, PhD, MPH, a DeWitt Wallace Distinguished Scholar at Weill Cornell Medical College.

Dr. Stevens, a prominent historian and policy analyst, completed her studies at Oxford and Yale universities, and has held professorships at Yale, Tulane, and Penn universities, in addition to her current faculty position at Weill Cornell Medical College. Dr. Stevens has published extensively in the fields of health policy research and the history of medicine, and has distinguished herself as a member of several national health policy committees on diverse topics, including Medicare, alternative medicine, and national blood policy. Currently, she is a member of the American Academy of Arts and Sciences and the Institute of Medicine. In her latest book, comprised of 17 annotated essays from her published and unpublished works as well as new commentaries, Dr. Stevens investigates such topics as civil rights in healthcare, government attitudes toward medical treatment for the poor, and health services research. Ultimately, her book stands as an examination of the nation's consistent struggle to balance government responsibility against the interests and efficiency of the private sector—a struggle that continues today and whose resolution, Dr. Stevens suggests, may be aided by an understanding of its history.



B. Timothy Walsh, MD

B. Timothy Walsh, MD, the William & Joy Ruane Professor of Pediatric

Psychopharmacology at Columbia University College of Physicians and Surgeons, recently authored 3 new books related to the treatment of adolescent mental health, particularly in the area of eating disorders.

Dr. Walsh, who has been a staff member at New York-Presbyterian Hospital/ Columbia University Medical Center since 1970, attended medical school at Harvard University. He served as the President of the Academy for Eating Disorders, and is now the Director of the Eating Disorders Research Unit at the New York State Psychiatric Institute. Dr. Walsh's first book, *Treating and Preventing Adolescent Mental Health Disorders: What We Know and What We Don't Know, a Research Agenda for Improving the Mental Health of Our Youth* (Oxford University Press, 2005), a large volume summarizing the results of these proceedings, won the 2005 Award for Excellence in Clinical Medicine. His second book, *If Your Child Has an Eating Disorder: An Essential Resource Guide for Parents* (Oxford University Press, 2005), is an easy-to-read guide for parents, teachers, and guidance counselors who are in close contact with adolescents. It explains the signs and symptoms of eating disorders and offers treatment suggestions and advice for every-day life for the families of affected teens. Dr. Walsh's third book, *Next to Nothing: A Firsthand Account of One Teenager's Experience With an Eating Disorder* (Oxford University Press, 2007), is co-authored with Carrie Arnold, an eating disorder sufferer, in an attempt to present a personalized account that is both accessible and informative to teenagers. The books all stemmed from the Adolescent Mental Health Initiative of the Annenberg Foundation Trust at Sunnylands, a project that aimed to examine the current understanding of adolescent mental health among both professionals and the general public.

New Research Elucidates Pathophysiology of Depression



Ramin V. Parsey, MD, PhD, and his team at NewYork-Presbyterian Hospital/Columbia University Medical Center have used positron emission tomography (PET) to make fundamental treatment discoveries for major depression and suicidality. Major depression is the most common mental illness.

“Our most immediate goal is to use these technologies to reduce the time people suffer by model-based treatment planning,” said Dr. Parsey.

He and colleagues recently conducted 2 studies that employed PET imaging to examine the serotonin (5-hydroxytryptamine, 5-HT) receptor 1A in depression and the serotonin transporter in depression. The studies,

Ottawa’s Ottawa Health Research Institute, who found a polymorphism of the promoter region of the 5-HT1A gene (*J Neurosci* 2006;26:1864-1871). His research has shown that subjects with the GG allele were more likely to be depressed and have suicidal ideation compared with subjects who do not have the allele. This prompted Dr. Parsey’s team to examine the effect of the polymorphism on protein expression in the brain in their subjects, using PET imaging. Specifically, they looked at all patients with the genotypes CC, CG, and GG.

Study findings revealed that patients who had more of the G allele showed more protein expression in the brain. “This suggests a model where you have a polymorphism. It creates increased

said Dr. Parsey. “I don’t think everyone with depression fits in this model.” He noted that many patients in the sample who were depressed did not have the GG polymorphism. “Perhaps there are abnormalities involving noradrenergic, dopaminergic, or multiple neurotransmitter systems,” he added.

They conducted another study showing that the 5-HT transporter was lower in the mid-brain and amygdala of people with depression compared with controls.

Currently, a prospective, NIMH-sponsored study is being conducted in which patients will receive exact doses of medications that only affect the 5-HT system. The team hopes to replicate findings in this study. “By that time, our statistician, R. Todd Ogdan, PhD, hopes to design a voxel-based logistic model, allowing us to assess the predictive capacity of the imaging, genetics, and other clinical/biological measures. We are aiming for a battery of tests that have high specificity and high sensitivity,” he said.

Historically, the investigators have used a ligand that was developed in 1995 and that measured both the high- and low-affinity states of the 5-HT1A receptors. They have since developed a ligand that measures just the high-affinity state of the receptor states.

If the imaging accounts for 50% of the predictive capacity, then the researchers

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“Our hope is that the information we gather can be useful to clinicians in diagnosis, treatment planning, or assessing suicidal risk in patients.”

—Ramin V. Parsey, MD, PhD

which were sponsored by the National Institutes of Mental Health (NIMH), found that depressed subjects who had never received antidepressant medications had higher 5-HT1A receptor levels than did healthy volunteers.

The researchers were familiar with the work of Paul Albert, PhD, a Senior Neuroscientist at University of

expression of the 1A receptor in the raphe nucleus. This may be related to studies that have shown that depression is associated with lower serotonin expression,” he said.

“We are excited because we can see the possible ramifications. But as a careful scientist, we have to make sure it is real before we present any solutions,”

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plan to develop a ligand and ship it to other centers. Currently, the team has a carbon 11 ligand, which has a 20-minute half-life. They hope to make a fluorinated compound, with a longer half-life and send it to other centers.

“Over the last 5 years, we have developed a novel molecule that binds just the 1A receptor in the high-affinity state,” he said. “We have completed structure–activity relationship studies, toxicology, and dosimetry, and we’re now looking for results of the first studies in humans. If that works, we’ll have an amazing new tool to look at functional 1A receptors,” he said.

The team at NewYork-Presbyterian/Columbia is also conducting studies on other neurological and psychological disorders, developing a variety of different ligands, and testing their models in genetically modified mice.

“Our goals are 2-fold,” said Dr. Parsey. “First, we want to understand

the pathophysiology of some forms of depression, and find out what, exactly, is wrong with the brain. And second, our hope is that the information we gather can be useful to clinicians in diagnosis, treatment planning, or assessing suicidal risk in patients.”

For more information on these and other studies, please visit <http://www.depression-studies.org>.

Ramin V. Parsey MD, PhD, is Director, Brain Imaging Core, Silvio O. Conte Center for the Neurobiology of Mental Disorders at NewYork-Presbyterian Hospital/Columbia University Medical Center and New York State Psychiatric Institute, Department of Molecular Imaging and Neuropathology, and is Associate Professor of Psychiatry at Columbia University College of Physicians and Surgeons. E-mail: rp242@columbia.edu.

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