

Schizophrenia and Manic- Depressive Disorder

THE BIOLOGICAL ROOTS OF MENTAL ILLNESS
AS REVEALED BY THE LANDMARK STUDY
OF IDENTICAL TWINS

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IN COLLABORATION WITH
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MANIC-DEPRESSIVE DISORDER

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and A. Thapar)

This book is dedicated to the twins and triplets who took part in the study. They unselfishly participated in extensive and sometimes uncomfortable testing so that research on schizophrenia and bipolar disorder could move forward. Without such individuals research is not possible, and we are all indebted to them.

All authors' royalties from this book have been assigned to the National Alliance for the Mentally Ill.

About the Authors

E. Fuller Torrey, M.D.: Dr. Torrey is a clinical and research psychiatrist in Washington, D.C., who specializes in schizophrenia and other serious mental illnesses. He has worked for the National Institute of Mental Health and St. Elizabeths Hospital in Washington, D.C., and has carried out field research on schizophrenia in Ireland and in Papua New Guinea. He has authored more than 200 professional publications, including 14 books. Among these are *Schizophrenia and Civilization*, *Surviving Schizophrenia: A Family Manual*, *The Roots of Treason*, *Nowhere to Go: The Tragic Odyssey of the Homeless Mentally Ill*, and most recently *Freudian Fraud: The Malignant Effect of Freud's Theory on American Thought and Culture*. Dr. Torrey directed the twin study.

Ann E. Bowler, M.S.: Ms. Bowler is a biostatistician presently employed as a clinical trial coordinator at the National Institute of Child Health and Development, the National Institutes of Health. She received her degree in biostatistics from Georgetown University in 1982 and has been a contributing author to more than 25 published papers. Ms. Bowler coordinated all the data collection and data analysis for the twin study.

Edward H. Taylor, Ph.D., A.C.S.W.: Dr. Taylor is currently on the faculty of the School of Social Work and the School of Medicine at the University of North Carolina at Chapel Hill. He has been recognized nationally for his writing and lecturing on the interaction between the biological, psychological, and social aspects of psychiatric illness. His interests center on

child and family studies, with an emphasis on the biological development of serious mental illness in children. Dr. Taylor was responsible for designing, administering, and interpreting data on the bio-psycho-social assessment of the twins, from the mothers' pregnancy to onset of illness.

Irving I. Gottesman, Ph.D., F.R.C. Psych. (Hon.): Dr. Gottesman is Commonwealth Professor of Psychology at the University of Virginia. Widely known for his work on genetics and schizophrenia, he is an Honorary Fellow of the Royal College of Psychiatrists and winner of the 1988 Stanley R. Dean Award for schizophrenia research and the 1990 Dobzhansky Award for lifelong contributions to behavioral genetics. He is the author of *Schizophrenia: The Epigenetic Puzzle* and *Schizophrenia Genesis: The Origins of Madness*, among other books. Dr. Gottesman was the senior consultant for the planning of the present research, participated in all diagnoses, and coordinated the analyses of personality tests to assess the effects of schizophrenia on personality.

Contributing Researchers

The following individuals contributed directly to the planning, testing, and data analysis for the project. However, the interpretation of the data in the following chapters is the responsibility of the authors alone and does not necessarily reflect the views of the contributing researchers.

I. Lead Researchers

Karen F. Berman, M.D.: Dr. Berman is Chief of the Unit on Positron Emission Tomography, NIMH Neuroscience Center at St. Elizabeths Hospital. She has specialized in neuroimaging studies and has authored over 100 professional publications. In 1986 she received the A. E. Bennett Foundation Award for Neuropsychiatric Research from the Society of Biological Psychiatry and in 1992 was awarded a U.S. Public Health Service Commendation Medal. Dr. Berman planned and carried out the PET scan and cerebral blood flow studies on the twins.

Llewellyn B. Bigelow, M.D.: Dr. Bigelow is a senior scientist in the Clinical Brain Disorder Branch, NIMH Neuroscience Center at St. Elizabeths Hospital. He has 25 years experience as a researcher on serious mental illnesses and is the author of more than 80 professional papers. In 1985 he received a Meritorious Service Award from the U.S. Public Health Service. Dr. Bigelow shared responsibility for all clinical measures and diagnoses of the twins.

H. Stefan Bracha, M.D.: Dr. Bracha, a child and adolescent psychiatrist and neuropsychiatrist, is Associate Professor of Psychiatry and Neurology at the University of Arkansas for Medical Sciences, Little Rock. He is an expert on prenatal brain development and dermatoglyphics and has written more than 50 articles about neurobiological brain disorders. He received clinical and research training at the Bronx VA Hospital, NIMH, and the University of California, San Diego. In 1989 he was awarded the Young Scientist Award by the National Alliance for the Mentally Ill. Dr. Bracha was responsible for research planning and data analysis of finger ridge counts and other dermatoglyphic measures in the twin study.

Richard Coppola, D.Sc.: Dr. Coppola is Chief of the Neuro-Imaging Unit, NIMH Neuroscience Center at St. Elizabeths Hospital. He has specialized in imaging techniques and the processing of neurophysiological data for studying brain activity. He has authored over 100 professional publications and been awarded a Commendation Medal and Outstanding Service Medal by the U.S. Public Health Service. Dr. Coppola was responsible for the collection of MRI and EEG data on the twins.

Terry E. Goldberg, Ph.D.: Dr. Goldberg, Chief of the Neuropsychology Unit, NIMH Neuroscience Center at St. Elizabeths Hospital, is one of the leading researchers in neuropsychology, especially in individuals with serious mental illnesses. He has published more than 100 professional papers and abstracts, including reviews of this research area. Dr. Goldberg was responsible for planning, coordinating, and analyzing the 3-hour battery of neuropsychological tests administered to the twins.

Thomas F. McNeil, Ph.D.: Dr. McNeil is Professor and Chairman of the Department of Psychiatry at the University of Lund, Sweden, where he has been associated since 1970. He has published many professional papers and book chapters on the relationship of obstetrical complications to serious mental illnesses and is a world authority on this subject. Prior to going to the University of Lund, Dr. McNeil was associated with the Lafayette Clinic in Detroit. Dr. McNeil was responsible for the data analysis on obstetrical complications in this study.

Patricia O. Quinn, M.D.: Dr. Quinn, Clinical Assistant Professor of Pediatrics and Child Psychiatry at Georgetown University School of Medicine, is in the private practice of developmental pediatrics. She has conducted research and published professional papers on minor physical anomalies for 20 years. She is also coauthor of *Putting on the Brakes: A Young People's Guide to*

Understanding Attention Hyperactivity Disorder, published in 1991. Dr. Quinn planned and carried out all examinations for minor physical anomalies.

Robert R. Rawlings, M.S.: Mr. Rawlings is a mathematical statistician with the Laboratory of Clinical Studies, National Institute of Alcohol Abuse and Alcoholism. He was trained in astrophysics and mathematics and is used as a consultant expert on statistical methodology and data analysis. He has been a contributor to more than 60 professional publications. Mr. Rawlings was the principal consultant for research design and statistical methodology for the twin study.

Kenneth C. Rickler, M.D.: Dr. Rickler, who is a neurologist with the Forensic Division at St. Elizabeths Hospital and a senior consultant to the NIMH Neuroscience Center, is also Clinical Associate Professor of Neurology and Clinical Assistant Professor of Psychiatry at the George Washington University School of Medicine. He has published many articles on neurological dysfunction in individuals with psychiatric illnesses and is an acknowledged authority in this field. Dr. Rickler planned the neurological examination and personally evaluated most of the twins in the study.

Daniel R. Weinberger, M.D.: Dr. Weinberger is Chief of the Clinical Brain Disorders Branch, NIMH Neuroscience Center at St. Elizabeths Hospital. Trained in both psychiatry and neurology, he is a leading researcher on neurobiological studies of serious mental illnesses and has been a major contributor to the recent explosion of knowledge in this area. He has authored more than 200 professional papers and coedited *The Neurology of Schizophrenia*. He was the recipient of the Judith B. Silver Award from the National Alliance for the Mentally Ill in 1985, the Foundations Fund Prize for Research from the American Psychiatric Association in 1991, and a Distinguished Service Medal from the U.S. Public Health Service in 1992. Dr. Weinberger planned and coordinated the MRI and cerebral metabolism studies of the twins.

Robert H. Yolken, M.D.: Dr. Yolken, Professor of Pediatrics and Director of the Division of Pediatric Infectious Diseases, Johns Hopkins University School of Medicine, is the author of close to 200 professional publications on viruses and viral diseases. In 1986 he received the Abbott Award from the American Society of Microbiology and in 1989 the E. Mead Johnson Award for Research in Pediatrics. Dr. Yolken coordinated the viral and immunological studies done on serum, lymphocytes, and cerebrospinal fluid from the twins.

II. Participating Researchers

Anisa Abi-Dargham, M.D., currently with the Department of Psychiatry, Yale University Medical Center, assisted with cerebral blood flow studies.

Alycia J. Bartley, B.A., currently a medical student, assisted with MRI analysis.

Elizabeth Cantor-Graae, M.S., Department of Psychiatry, University of Lund, Sweden, assisted with analysis of obstetrical complications.

Nicholas W. Carosella, M.D., is with the Allegheny Neuropsychiatric Institute in Pittsburgh and assisted with MRI analysis.

Constance Carpenter, Ph.D., NIMH Neuroscience Center, assisted with neuropsychological testing.

Manuel F. Casanova, M.D., Professor of Psychiatry and Neurology at the Medical College of Georgia, assisted with MRI analysis.

George W. Christison, M.D., currently with the Department of Psychiatry, Loma Linda University, assisted with MRI analysis.

David G. Daniel, M.D., who is with Dominion Hospital in Falls Church, Virginia, assisted with cerebral blood flow studies.

David L. DiLalla, Ph.D., Department of Psychology, Southern Illinois University, assisted with analysis of the psychological data pertaining to personality traits of the twins.

Paula Domenici, B.A., who will be starting a graduate program in psychology, assisted with data analysis of the neuropsychological tests.

Darlene R. Doshen, NIMH Neuroscience Center, assisted with the collection of dermatoglyphics.

James M. Gold, Ph.D., NIMH Neuroscience Center, assisted with neuropsychological testing and analysis.

Julie G. Gorey, M.A., NIMH Neuroscience Center, assisted with the cerebral blood flow studies.

Monica Gourovitch, Ph.D., NIMH Neuroscience Center, assisted with neuropsychological testing and analysis.

Ronald L. Green, M.D., Department of Psychiatry, Dartmouth Medical Center, assisted with MRI analysis.

Edmund S. Higgins, M.D., currently with the Department of Psychiatry, Medical University of South Carolina, assisted with the analysis of obstetrical data.

Thomas M. Hyde, M.D., Ph.D., NIMH Neuroscience Center, assisted with neurological and EEG testing.

Douglas W. Jones, Ph.D., NIMH Neuroscience Center, assisted with the MRI, SPECT, and PET testing.

- Henrietta Kulaga, Ph.D., NIMH Neuroscience Center, assisted with immunological and virological studies.
- Jennifer J. Kulynych, M.A., a doctoral candidate in psychology at American University, assisted with MRI analysis.
- Robert E. Litman, M.D., Section on Clinical Studies, NIMH Intramural Research Program, conducted the studies of eye tracking.
- Laura Marsh, M.D., currently with the Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, assisted with MRI analysis.
- Henry McFarland, M.D., National Institute of Neurological Diseases and Stroke, coordinated the collection and testing of lymphocytes.
- Michael S. Myslobodsky, M.D., D.Sc., Department of Psychology, Tel Aviv University, Israel, assisted with MRI analysis.
- J. Thomas Noga, M.D., NIMH Neuroscience Center, assisted with MRI analysis.
- Jill L. Ostrem, B.A., NIMH Neuroscience Center, assisted with cerebral blood flow studies.
- Mihael H. Polymeropoulos, M.D., NIMH Neuroscience Center, coordinated genetic DNA studies of the twins using minisatellite probes.
- J. Daniel Ragland, Ph.D., currently an assistant professor in the Department of Psychiatry, University of Pennsylvania, assisted with neuropsychological testing and analysis.
- Mark H. Rapaport, M.D., Department of Psychiatry, University of California at San Diego School of Medicine, assisted with the immunologic studies.
- Susan M. Resnick, Ph.D., Gerontology Research Center, National Institute on Aging, carried out some of the cerebral blood flow studies.
- Angelo Sambunaris, M.D., NIMH Neuroscience Center, assisted with immunologic studies.
- Roy H. Sexton, B.S., NIMH Neuroscience Center, assisted with cerebral blood flow studies.
- Karin Sjostrom, M.D., Department of Psychiatry, University of Lund, Sweden, assisted with analysis of the obstetrical data.
- Hans H. Stassen, Ph.D., Psychiatric University Hospital, Zurich, Switzerland, is analyzing the EEG data.
- Richard L. Suddath, M.D., currently with Centennial Peaks Hospital, Louisville, Colorado, assisted with MRI analysis.
- Alejandro Terrazas, B.S., President of Terrazas Analytical Systems in Washington, D.C., assisted with data analysis.
- Katalin Vldar, M.D., a National Fogarty Fellow at NIMH, assisted with MRI analysis.

Ivan N. Waldman, M.S., NIMH Neuroscience Center, assisted with data analysis and computer programming.

Jeffrey R. Zigun, M.D., currently with the Department of Psychiatry, Medical College of Wisconsin, assisted with MRI analysis.

Mark Zito, M.S., NIMH Neuroscience Center, assisted with MRI analysis.

Preface

THIS BOOK reports the findings of a 6-year study of schizophrenia and bipolar disorder in 66 pairs of identical twins. The study was funded primarily by the National Institute of Mental Health and cost in total just over \$1 million for the 6 years.

Although data from the study are still being analyzed, the vast majority of preliminary analyses have been completed. We therefore decided to publish the findings to date, since neuroscience research is moving so rapidly ahead in this decade of the brain. The largest data sets unanalyzed are the electroencephalographs (EEGs). Data analyses are also continuing on MRI, PET, and eye-tracking findings. In addition, genetic, immunological, and virological studies are continuing on the serum, lymphocytes, and cerebrospinal fluid collected from the twins. It is likely, in fact, that these analyses will continue for several more years because identical twins provide such a unique opportunity for understanding these diseases.

The twins are not identified by name in the book. Personal facts have been slightly altered in a few narratives to ensure anonymity.

It may be questioned whether the results of this study of identical twins with schizophrenia and bipolar disorder are applicable to non-twins with these diseases. Most researchers have assumed that they are, and recently this fact was confirmed. Twins with schizophrenia and bipolar disorder in the Maudsley twin register in London were compared with non-twins with the same diagnoses. No clinical differences

were found between the twins and the non-twins, or between identical and fraternal twins (Marshall et al., 1993). It is reasonable to assume, therefore, that the results of the present study are applicable to non-twins with these diseases.

Acknowledgments

THE LOGISTICS involved in bringing 66 twin pairs to Washington, D.C., for evaluation and testing are fearsome. The research was accomplished with the exceptional cooperation and help from many people. Camille DiRienzo-Callahan coordinated the logistics for 5 years with unsurpassed enthusiasm, and Theresa Kordestani capably managed the office for the final year. Iva Chambers, Helen Ball, and Joseph Navarro selflessly served as driver-escorts for the twins for the entire length of the project. Richard H. Meacham, Patrick Bogan, Eleanor Bruns, and Wanda Cross of Friends Medical Science Research Center in Baltimore administered the funds for the project, minimizing administrative headaches for the researchers and providing exemplary support. David Shore at the NIMH Schizophrenia Research Branch provided crucial guidance and encouragement as we tried to decipher federal grant regulations, and Lou Ellen Rice of NIMH was most helpful in administering our NIMH contract.

The NIMH Neuroscience Center at St. Elizabeths Hospital generously provided us with space and support, and for this we are indebted to Rex Cowdry, Richard J. Wyatt, Daniel R. Weinberger, and Joel E. Kleinman. Richard Staub, Mollie Strotkamp, Theresa Tolbert, Delores Freeman, Joyce Williams, Leroy Sundberg, Kyle Christiansen, Laverne Corum, and Dera Tompkins were all graciously responsive to our needs. Diane Venable and Thomas Bryant assisted us with laboratory work, and Barry Sydnor provided computer assistance. Mary Herman kindly reviewed portions of the manuscript.