

Clinical and Genetic Epidemiology

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Overview

The Division of Clinical & Genetic Epidemiology was established in 1987 to gain understanding of the rates and risk factors primarily of mood and anxiety disorders (using methods of epidemiology and genetics), and to apply these findings to develop and test empirically based interventions. As new findings, evolving interests, and new technology have been introduced, the research has extended to include neuro-psychological and brain imaging studies; health services research, a section in mathematical genetics which includes a research and training program to strengthen statistical methods in genetic studies. The research falls into three areas: Genetics/High-risk; Epidemiology/Health Services; and Clinical intervention/Prevention. All studies are supported by the Division's data management section, expert statistical consultation, and standardized diagnostic training services. Numerous collaborations both within the Medical Center and outside make this diverse work possible.

The extent and breadth of our research can best be summarized by the current funded grants, which include a total of 29 from NIH, private foundations, and pharmaceutical companies. Last year our group published 44 papers in scientific journals. We have chosen to focus our clinical studies on improving the mental health care of the poorest and often the most underserved populations, patients in primary care, and students in school based clinics. We have been selected by NIMH along with Howard University as a site to recruit the first large sample of African Americans to participate in a

genetic study of early onset recurrent depression. This is a group largely underrepresented in research studies.

Current Research

Pal and Greenberg identified a major gene for adolescent-onset epilepsies, malic enzyme 2; showed that myoclonic and absence seizures are inherited separately in idiopathic generalized epilepsies and presented evidence that social support can be both a risk and a protective factor for child behavioral outcomes.

Genetics/High Risk

The offspring of depressed parents have high rates of depression and considerable impairment. How to intervene and change this course has not been clear. Weissman, Wickramaratne, Pilowsky, and STAR*D collaborators assessed the children of mother's undergoing treatment for depression. JAMA (March 2006) called a press conference to report study results which showed that successful treatment of the mother's depression to remission resulted in a significant decrease in their children's psychiatric disorders. Lack of remission resulted in either no change, or new episodes in the children. These reports received wide converge on national TV, radio, and the press including the *Washington Post*, *Wall Street Journal*, and the front page of *USA Today* and has helped to generate national interest in how to improve the quality of care for depressed mothers. The Institute of Medicine is calling for a study to direct health policy in the treatment of maternal depression.

Population stratification can seriously hamper case control genetic association studies. Hodge, Greenberg, and colleagues presenting a new method to correct for population stratification which had superior properties, compared to other methods in the literature. Evidentialism is an alternative statistical paradigm that is more appropriate for scientific inference than the standard "p-value" approach. The concept hadn't been applied to genetic studies. In two groundbreaking papers, Hodge and Strug applied this approach to genetic studies and examined the implications for dealing with the knotty "multiple testing" problem that bedevils genome wide scans.

Weissman and colleagues as part of a multi-centered subpair study of early onset recurrent major depression reported on a genome wide linkage scan based in over 1400 informative affected relative pairs. Regions on chromosome 15q, 17p, and 8p might contain that genes contribute to susceptibility to major depression. Evidence for linkage has been reported independently in the same region of chromosome 15q for major depression and of chromosome 8 for related personality disorders. This grant has been refunded for an additional 4 years.

In a longitudinal high-risk study, Bruder, Warner, Tenke, Weissman and colleagues reported that offspring with both parents having a major depression showed an EEG alpha asymmetry at parietotemporal sites resembling that previously reported for depressed adolescents and adults. This EEG alteration may represent a biological marker of vulnerability to a familial form of depression.

Greenberg, D. Multicenter Study of Idiopathic Generalized Epilepsy, NINDS/RO1 NS27941

Greenberg, D. Two-locus Models: Heterogeneity and Diabetes, NIDDK/RO1 DK31755

Hodge, S. Linkage and Segregation in Complex Genetic Diseases, NIDDK/RO1 DK21313

Hodge, S. Genetic Analysis: Psychiatric and Other Complex Diseases, NIMH/T32 MH65213

Hodge, S. Psychiatric Genetics and Family Studies: Robust Methods, NIMH/RO1 MH48858

Murphy, E. (Weissman: Mentor). NARSAD Junior Investigator Award, Investigating the Challenges of Recruiting Ethnic Minorities in Genetic Research, NARSAD Junior Investigator Award

Weissman, M. Children and High and at Low Risk for Depression, NIMH/RO1 MH36197 (This now includes a NIDA supplement: Risk of Substance Use and Abuse: A Three-Generation Study)

Weissman, M. Genetics of Recurrent Early-Onset Major Depression NIMH/RO1 MH60912

Weissman, M. Three Generations at Risk or Depression: Genetic Studies, NARSAD Distinguished Investigator Award

Weissman, M. Genetic Studies of Depressive Disorders, NIMH/RO1 MH28274

Weissman, M. Genetic Studies of High Risk Families, Sackler Foundation

Weissman, M. Clinical Studies of Human Anxiety Disorders, NIMH/RO1 MH060970

Epidemiology/Health Services

Olfson and coworkers reported (*Archives of General Psychiatry*) a sharp national increase in antipsychotic treatment of children and adolescents with a variety of mental disorders. Office-based medical visits by children and adolescents that included antipsychotic medications increased from approximately 201,000 in 1993 to 1,224,000 in 2002. During 2000-2002, a larger proportion of the child and adolescents visits with antipsychotic medications were to treat disruptive behavior disorders or mood disorders than developmental disorders or psychotic disorders. This study was widely covered in the media, including the *New York Times*, *CNN*, and *National Public Radio*, and helped to generate a national discussion of the quality of antipsychotic treatment in young people.

Young people commonly present to emergency departments following attempted suicide. Although psychiatric epidemiologic studies indicate that over 95% of young people meet criteria for one or more mental disorders at the time of attempted suicide, little is known about the emergency room assessment and management of suicidal youth in community emergency departments. Olfson and colleagues examined the emergency room assessment and management of a nationally representative sample of young people following attempted suicide. The results, which were reported in the *Archives of General Psychiatry* (October 2005) and were widely covered in the medical and lay press, indicated that mental disorders are diagnosed in only about one-half (56%) of emergency department visits by young people following a suicide attempt. These findings highlight that a pressing national need exists for systematic mental health assessments of young people who present to emergency departments following attempted suicide.

Little information exists on the long-term effects of 9/11 in high-risk clinical populations. Neria, Weissman, Olfson, and colleagues found minority, low-income primary care patients in Northern Manhattan had high rates of PTSD both in the mid term (10%: one year after 9/11) and the long term (6%: approximately 4 years after 9/11). High impact exposure in 9/11 (e.g., knowing somebody who was killed in 9/11) resulted in a broad range of psychopathology 4 years after the attacks. These findings highlight the specific needs for health care associated with long term post-disaster psychopathology among high risk populations and underscore the importance of developing post-trauma professional care, including screening and treatment capacities for individuals exposed to trauma in general medical practices.

Neria, Y. Long Term Impact of the World Trade Center Attacks in Primary Care, NIMH/R01 MH 72833

Neria, Y. (Weissman: Mentor). Depression and PTSD in Primary Care Patients Exposed to the World Trade Center Attack, NARSAD Junior Investigator Award

Olfson, M. SSRI Treatment and Suicide in Depressed Youth, NARSAD Distinguished Investigator Award

Olfson, M. Economic Consequences of Relapse in Schizophrenia, Lilly

Olfson, M, Subcontract on AHRQ Center for Education and Research on Mental Health Therapeutics, ML Crismon, PI Rutgers Univ.

Olfson, M. Depression, Somatic Pain, and Health Care Costs, Lilly

Olfson, M. Mental Health in: Columbia Center for the Health of Urban Minorities (CHUM) O Carrasquillo PI, MCMHD #MD00206 P60 Core 7

Olfson, M. Suicide Prevention Through Treatment of Depression, American Foundation for Suicide Prevention

Olfson, M. Antipsychotic Associated Hyperlipidemia, Bristol Meyers Squibb

Olfson, M. Clinical Review of Issues in the Presentation, Recognition, Diagnosis, and Management of Depression in Adult Hispanics, Lilly

Weissman, M. Characteristics of Bipolar Depression in Primary Care, Lilly

Weissman, M. Course of Major Depression in a Low Income Primary Care Practice, Glaxo-Smith Kline

Clinical Intervention/Prevention

Verdeli, Wickramartne, Weissman, and colleagues reported that 16 week group interpersonal psychotherapy applied in a randomized trial to depressed patients in Uganda continued to confer benefits at 6 month follow-up after conclusion of the formal intervention.

Mufson, L. Group IPT-A in School-based Clinics, NIMH/RO1 MH076340

Verdeli, H. Prevention for Symptomatic Offspring of Bipolar Parents, NIMH/ K23 MH071530

Verdeli, H. A Prevention Intervention for Symptomatic Adolescent Children of Mothers with Bipolar Disorder, NARSAD Junior Investigator Award

Verdeli, H. Interpersonal Psychotherapy (IPT) for Adolescents of Bipolar Mothers: A Randomized Clinical Trial, Sol Goldman Charitable Trust

Weissman, M. Children of Depressed Mothers: STAR*D Ancillary Study, NIMH/RO1 MH 63852

Weissman, M. Bridging the Gap Between Research and Clinical Practice of Modern Psychotherapy, Josiah Macy Foundation

Education and Training

We have numerous education and training activities. Sue Hodge's NIMH training program in statistical genetics has a community of 4 graduate students, 6 post-doctoral fellows, and faculty, who meet on a regular basis. Eight PhD or MPH, graduate students in social work, epidemiology, socio-medical sciences or biostatistics; 6 postdoctoral fellows, 4 psychiatric residents including a psychiatric resident who spent 6 months with us in an elective from Harlem Hospital and a visiting postdoctoral fellow from Thailand were part of our Division. A scientist psychiatrist from Israel spent a sabbatical with us. We have one K-awardee. Our staff is highly sought after nationally and internationally to train in evidenced psychotherapy, e.g. British Columbia, Finland Ministry of Health, NY State Office of Mental Health, (Mufson); Gao, Uganda, Greece, China, India (Verdeli). Weissman supervised a psychiatric resident in IPT and participated in a course in IPT for PGY3.

Awards/Honors

Randy Semple, PhD, Eleanor Murphy, PhD, and Julian Manetti-Cusa, PsyD passed their psychology licensure exams. Priya Wickramaratne, PhD and Mark Olfson, MD were appointed to NIMH Scientific Review Committees.

Grants

| Principal Investigator/ Project Director | Funding Agency/ Grant # | Title | Project Period | Total Direct Costs (\$) |
|---|---|--|----------------|-------------------------|
| Greenberg, David | NINDS/R01 NS27941 | <i>Multicenter Study of Idiopathic Generalized Epilepsy</i> | 2006-2011 | |
| Greenberg, David | NIDDK/R01 DK31775 | <i>Two-locus Models, Heterogeneity and Diabetes</i> | 2003–2007 | 125,000 |
| Hodge, Susan | NIDDK/R01 DK31813 | <i>Linkage and Segregation in Complex Genetic Diseases</i> | 2003–2008 | 425,000 |
| Hodge, Susan | NIMH/T32 MH65213 | <i>Genetic Analysis: Psychiatric and Other Complex Diseases</i> | 2002–2007 | 751,855 |
| Hodge, Susan | NIMH/2R01 MH48858 | <i>Psychiatric Genetics and Family Studies: Robust Methods</i> | 2006-2011 | 743,750 |
| Mufson, Laura | NIMH/1R01 MH076340 | <i>Group IPT-A in School-based Clinics</i> | 2005-2010 | 3,023,565 |
| Murphy, Eleanor (Weissman, Mentor) | NARSAD Junior Investigator Award | <i>Investigating the Challenges of Recruiting Ethnic Minorities in Genetic Research</i> | 2005-2007 | 60,000 |
| Neria, Yuval | NIMH/1R01 MH72833 | <i>Long Term Impact of the World Trade Center Attacks in Primary Care</i> | 2005–2008 | 934,205 |
| Neria, Yuval (Weissman, Mentor) | NARSAD Junior Investigator Award | <i>Depression and PTSD in Primary Care Patients Exposed to the World Trade Center Attack</i> | 2003–2005 | 60,000 |
| Olfson, Mark | NIMH/R01 MH61530 | <i>Medication Management Decisions in Schizophrenia</i> | 2001–2006 | 794,782 |
| Olfson, Mark | NARSAD Distinguished Investigator Award | <i>SSRI Treatment and Suicide in Depressed Youth</i> | 2005-2007 | 92,593 |
| Olfson, Mark | Lilly | <i>Economic Consequences of Relapse in Schizophrenia</i> | 2005-2006 | 79,974 |
| Olfson, Mark | Lilly | <i>Depression, Somatic Pain, and Health Care Costs</i> | 2004–2006 | 46,145 |

| Principal Investigator/ Project Director | Funding Agency/ Grant # | Title | Project Period | Total Direct Costs (\$) |
|---|---|--|-----------------------|--------------------------------|
| Olfson, Mark | NCMHD #MD00206 P60 | <i>Core 7, Mental Health in: Columbia Center for the Health of Urban Minorities (CHUM) O Carrasquillo, PI</i> | 2003–2008 | 392,403 |
| Olfson, Mark | American Foundation for Suicide Prevention | <i>Suicide Prevention Through Treatment of Depression</i> | 2004–2007 | 99,919 |
| Olfson, Mark | Bristol Meyers Squibb | <i>Antipsychotic Associated Hyperlipidemia</i> | 2004-2005 | 74,407 |
| Olfson, Mark | Lilly | <i>Clinical Review of Issues in the Presentation, Recognition, Diagnosis, and Management of Depression in Adult Hispanics.</i> | 2003–2005 | 15,000 |
| Olfson, Mark | BMS | <i>Aripirazole dosing and titration in the community management of schizophrenia and bipolar disorder</i> | 2006-2007 | 168,388 |
| Olfson, Mark | Lilly | <i>Treatment of Schizophrenia with long acting Fluphenazine, Halperidol, or Risperidone</i> | 2005-2007 | 80,043 |
| Olfson, Mark | BMS | <i>Antipsychotic Discontinuation and Hospital Admission in Antipsychotic-Treated Bipolar Patients</i> | 2006-2007 | 64,034 |
| Olfson, Mark | Subcontract from Rutgers on AHRQ Grant U18 HS016097 | <i>Center for Education and Research on Mental Health Therapeutics</i> | 2006-2011 | 570,832 |
| Verdeli, Helena | NIMH/ K23 MH071530 | <i>Prevention for Symptomatic Offspring of Bipolar Parents</i> | 2005 2010 | 828,480 |
| Verdeli, Helena | NARSAD Junior Investigator Award | <i>A Prevention Intervention for Symptomatic Adolescent Children of Mothers with Bipolar Disorder</i> | 2000–2005 | 60,000 |
| Verdeli, Helena | Sol Goldman Charitable Trust | <i>Interpersonal Psychotherapy (IPT) for Adolescents of Bipolar Mothers: A Randomized Clinical Trial</i> | 2003–2007 | 80,000 |
| Weissman, Myrna | NIMH/R01 MH36197 | <i>Children at High and at Low Risk for Depression</i> | 2003–2007 | 2,958,660 |
| | Admin supplement to above from NIDA | | 2006-2007 | 267,071 |

| Principal Investigator/ Project Director | Funding Agency/ Grant # | Title | Project Period | Total Direct Costs (\$) |
|---|---|---|---------------------------|--------------------------------|
| Weissman, Myrna | NIMH/P30 MH071478 | <i>Principal Research Core of ACISR for Pediatric Psychiatry Disorders (David Shaffer, PI) (Myrna Weissman, Core PI)</i> | 2004–2009 | 1,274,194 |
| Weissman, Myrna | NIMH/R37 MH28274 | <i>Genetic Studies of Depressive Disorders</i> | 2002–2006 | 529,826 |
| Weissman, Myrna | Sackler | <i>Three Generations at Risk for Depression: Genetic Studies</i> | 2005-2006 | 100,000 |
| Weissman, Myrna | NIMH/R01 MH63852 | <i>Children of Depressed Mothers: A STAR*D Ancillary Study</i> | 2001–2007 | 3,939,150 |
| Weissman, Myrna | NIMH/P01 MH060970 | <i>Clinical Studies of Human Anxiety Disorders, a Project of the PPG Molecular Genetic Study of Fear and Anxiety, (Rene Hen, PI) (Myrna Weissman, Project PI)</i> | 2003–2007 | 900,948 (project only) |
| Weissman, Myrna | NIMH/R01 MH60912 | <i>Genetics of Recurrent Early-Onset Major Depression</i> | 2005–2009 | 1,346,512 |
| Weissman, Myrna | NARSAD Distinguished Investigator Award | <i>Three Generations at Risk for Depression: Genetic Studies</i> | 2005-2007 | 92,593 |
| Weissman, Myrna | Lilly/F1D-US-X271 | <i>Characteristics of Bipolar Depression in Primary Care</i> | 2004–2006 | 120,000 |
| Weissman, Myrna | GlaxoSmithKline | <i>Course of Major Depressive Disorder in a Low Income Primary Care Practice</i> | 2005-2006 | 60,000 |
| Weissman, Myrna | Lilly | <i>Clinical Review of Issues in the Presentation, Recognition, Diagnosis and Management of Depression in Adult African Americans</i> | 2003–2005 | 15,000 |
| Weissman, Myrna | NIMH/T32 MH16434 | <i>Research Training in Child Psychiatry (D. Shaffer, PI,)</i> | 2005–2010 | 561,740 |
| Weissman, Myrna | Sackler | <i>Sackler Institute for Developmental Psychobiology (Myron Hofer, Director, Weissman, Director of Clinical Division)</i> | 2002 – no set termination | 40,000/year |

| Principal Investigator/ Project Director | Funding Agency/ Grant # | Title | Project Period | Total Direct Costs (\$) |
|---|----------------------------|--|----------------|-------------------------|
| Weissman, Myrna | Josiah Macy Jr. Foundation | <i>Bridging the Gap Between Research & Clinical Practice of Modern Psychotherapy</i> | 2003–2006 | 200,000 |

Publications

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