

A genome-wide search for chromosomal loci linked to mental health wellness in relatives at high risk for bipolar affective disorder among the Old Order Amish

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ABSTRACT Bipolar affective disorder (BPAD; manic-depressive illness) is characterized by episodes of mania and/or hypomania interspersed with periods of depression. Compelling evidence supports a significant genetic component in the susceptibility to develop BPAD. To date, however, linkage studies have attempted only to identify chromosomal loci that cause or increase the risk of developing BPAD. To determine whether there could be protective alleles that prevent or reduce the risk of developing BPAD, similar to what is observed in other genetic disorders, we used mental health wellness (absence of any psychiatric disorder) as the phenotype in our genome-wide linkage scan of several large multigeneration Old Order Amish pedigrees exhibiting an extremely high incidence of BPAD. We have found strong evidence for a locus on chromosome 4p at D4S2949 (maximum GENEHUNTER-PLUS nonparametric linkage score = 4.05, $P = 5.22 \times 10^{-4}$; SIBPAL $P_{\text{multipoint}}$ value $<3 \times 10^{-5}$) and suggestive evidence for a locus on chromosome 4q at D4S297 (maximum GENEHUNTER-PLUS nonparametric linkage score = 3.29, $P = 2.57 \times 10^{-3}$; SIBPAL $P_{\text{multipoint}}$ value $<1 \times 10^{-3}$) that are linked to mental health wellness. These findings are consistent with the hypothesis that certain alleles could prevent or modify the clinical manifestations of BPAD and perhaps other related affective disorders.

Bipolar affective disorder (BPAD) afflicts approximately 1% of the population and is associated with a high risk of suicide (1). Twin, family, and adoption studies have provided strong evidence for an important genetic component in the susceptibility to develop BPAD (2), but unlike for other common medical illnesses, robust biological markers have not been identified for BPAD, and genetic linkage studies have had to rely on categorical diagnoses. Genetic heterogeneity, phenocopies, genotyping errors, and the complexities of performing and interpreting statistical analyses may contribute to some of the inconsistencies observed in these linkage studies (3–12). However, because the inheritance of BPAD is probably multifactorial, the possible involvement of multiple genetic components of small effect and/or the occurrence of major allelic effects only in epistasis must be considered. We previously have suggested (13), that in

addition to susceptibility alleles, there could be alleles that reduce the risk of developing BPAD in a manner similar to that reported for other complex genetic disorders. If model-based linkage analyses are used, a false-negative linkage finding could result when individuals inherit disease susceptibility alleles but do not manifest the phenotype because of the presence of protective alleles. The inclusion of individuals who inherit susceptibility alleles but do not manifest disease because of protective alleles, or of individuals who inherit protective alleles but nevertheless manifest the disease, also will reduce the power of model-free (allelic-sharing) analyses. Thus, regardless of whether model-based or model-free analyses are used, wellness or protective alleles could have a significant impact on linkage analyses.

Ascertainment of psychiatric disorders and health among several large multigenerational Old Order Amish pedigrees covers a period of more than 20 years. Throughout this longitudinal study, procedures for assessing and diagnosing subjects have remained constant and have included a thorough evaluation of all bipolar I (BPI) probands and their relatives (14–16). Morbid risk analyses have demonstrated a high prevalence of affective disorder among first-degree relatives of bipolar probands in these families (17). Because of the long-term, longitudinal nature of the study, the unaffected, mentally healthy individuals in these families also were followed, many for a period of years past the age of risk for BPAD. Consequently, rather than limit our genome-wide search to identifying susceptibility loci for the disease phenotype (BPAD), we tested the hypothesis that protective alleles may contribute to the absence of psychiatric illness (i.e., mental health wellness) in unaffected family members in these high-risk pedigrees. Because the mode of inheritance of any gene(s) modifying the relative risk for affective disorder is unknown (2) we relied exclusively on model-free linkage analyses. We now report strong evidence for linkage of DNA markers on chromosome 4p to mental health wellness in relatives at high risk for, but who did not develop, major affective disorder in several large multigenerational Old Order Amish pedigrees with an extremely high incidence of BPAD.

Abbreviations: BPAD, bipolar affective disorder; NPL, nonparametric linkage; BPI, bipolar I; GH-PLUS, GENEHUNTER-PLUS; IBD, identical by descent.

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Relatives At Risk For Mental Disorder

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Relatives At Risk For Mental Disorder:

Relatives at Risk for Mental Disorder David L. Dunner, Elliot S. Gershon, James Elmer Barrett, 1988 **How to Talk with Families About Genetics and Psychiatric Illness** Holly Landrum Peay, Jehannine Claire Austin, 2011-01-17

Addressing clients questions and concerns about the role of genetics in mental illness As we learn more about how our biology and genes can play into the development of a mental health disorder patients and their families are increasingly seeking answers to tough questions about common risk factors the likelihood of recurrence the need for genetic testing and implications for future generations A practical go to resource for all mental health clinicians this guide explains just how to address these questions and concerns in a way that is comprehensible and compassionate Filled with case studies sample dialogues and question and answer examples it is an essential roadmap for practitioners helping them to demystify a complex issue for their clients and equip them with the accurate reassuring information they need **California. Court of Appeal (2nd Appellate District). Records and Briefs** California (State)., Received document entitled EXHIBITS **Handbook of Mental Health and Aging** James E. Birren, Gene D. Cohen, R. Bruce Sloane, Barry D. Lebowitz, Donna E. Deutchman, May Wykle, Nancy R. Hooyman, 2013-10-22 This book is a thorough revision of one of the most comprehensive reference volumes for persons working in the area of aging and mental health The thrust of the work is interdisciplinary and discusses research on both clinical and practical issues in aging and mental health The multidisciplinary nature of this book and the inclusion of subject matter from the professional as well as research realm result in a level of comprehensiveness which is distinct in the field of mental health and aging Each chapter contains a comprehensive bibliography the compilation of which represents a definitive reference source in the field The chapters review state of the art research in the biological behavioral and social sciences and represent the cutting edge of current practice in psychiatry neurology social work nursing psychology and pharmacology among other professions The compilation of prevalence data is a much needed addition to the current literature The multidisciplinary nature of this book and the inclusion of both clinical and practical issues makes the book distinctively comprehensive *Evidence-based Policy and Practice in Mental Health Social Work* Martin Webber, 2011-07-11

Mental health social workers work within multidisciplinary teams often based in health settings The variety of services they work within are shaped by mental health policy that is increasingly being influenced by research evidence of what works This fully revised second edition has a new chapter on systematic reviews and greater coverage of the impact of the 2007 amendment to Mental Health Act 1983 on mental health practitioners and services *Violent Behavior and Mental Illness* American Psychiatric Association, Carl C. Bell, 1997 The book is a compendium of articles from Psychiatric Services and Hospital and Community Psychiatry on violent behavior and mental illness *Public Mental Health* William W. Eaton, M. Daniele Fallin, 2019-04-03 A masterful volume that will do much to advance understanding of mental health as an essential public health challenge Journal of Sociology Social Welfare THE GROUNDBREAKING TEXTBOOK IN POPULATION LEVEL

MENTAL HEALTH NOW FULLY REVISED AND UPDATED Public Mental Health equips a new generation of public health students researchers and practitioners with the most innovative social biological and behavioral science approaches to mental health challenges at the population level Incorporating insights from multiple health and science disciplines this new edition introduces novel concepts and methodologies for understanding the occurrence of mental disorders in populations worldwide Reflecting the disciplinary diversity and expertise of an internationally recognized roster of contributors its nineteen chapters include coverage of such essential topics as estimates of global prevalence based on new data from the Global Burden of Disease Study the complex way in which genes other biological factors and life stresses increase risk mental health disparities among population subgroups population level mental health consequences of violence and natural disasters the logic and practice of prevention of mental and behavioral disorders With a perspective that will resonate from the lab to the legislature floor Public Mental Health offers a much need core text for students researchers and practitioners

Recognition and Prevention of Major Mental and Substance Use Disorders American Psychopathological Association, 2007-05-03 Recognizing that favorable clinical outcomes are associated with earlier initiation of treatment and even more ideally with prevention this volume addresses the current status of early intervention in and prevention of major mental and substance use disorders A team of distinguished participants addresses this problem at many levels from the DNA molecule to public policy in order to show how prevention efforts should be informed by a better understanding of etiology and by a knowledge of indicators of vulnerability In considering the current standing of etiological knowledge Recognition and Prevention of Major Mental and Substance Use Disorders addresses issues that are critical precursors to the prevention of mental disorders and offers an understanding of factors that contribute to the disorders development The contributors review genetic methodologies and current findings in mental disorders with an emphasis on schizophrenia and then show how biological and psychosocial environmental variables may affect vulnerability Chapters devoted specifically to lessons in prevention drawn from recent research into schizophrenia discuss the implications of prodromal studies and relationships between stress critical periods and the development of the disorder The book includes contributions from NIH representatives on how basic scientific understanding of mental disorders can be translated into public policy It also features chapters that describe cutting edge projects in prevention research for Alzheimer s disease drug dependence antisocial behavior and posttraumatic stress disorder each providing compelling accounts of how existing knowledge can be adapted to promising prevention efforts Among the volume s contributions New data on the role of substance abuse particularly marijuana and psychostimulants in increasing vulnerability to schizophrenia Review of vulnerability factors for several relevant disorders examining stress and its concomitant psychobiological responses and the contribution of cognitive factors to vulnerability to depression Intriguing approach for translating successful treatment methods for schizophrenia into efforts to prevent the transition from the prodrome of the disorder to the full blown illness Program for prevention of antisocial

behavior that can be implemented as early as the first grade Secondary prevention efforts for posttraumatic stress disorder with a focus on pharmacological interventions Each chapter reviews clinical implications of the research presented contributing to a volume that will benefit clinicians and researchers who share the goal of preventing these debilitating conditions This multidimensional interdisciplinary work represents a major step toward cutting the social costs of these disorders and more important their untold cost in human suffering

A Life Course Approach to Mental Disorders Karestan C. Koenen, Sasha Rudenstine, Ezra Susser, Sandro Galea, 2013-10 A Life Course Approach to Mental Disorders examines the causes and consequences of a wide range of mental disorders throughout life from the peri natal period through old age

Mental and Neurological Public Health Vikram Patel, Alistair Woodward, Valery Feigin, Stella R. Quah, Kristian Heggenhougen, 2010-06-07 Colin Mathers who leads the Global Burden of Disease group in WHO has confirmed that in the 2004 GBD 13 1% of global Daily Adjusted Life Years are attributable to mental or neurological disorders While the proportions vary very widely from about 10% in low income countries to over 25% in high income countries it is clear that there is a need for understanding how to address this issue This volume aims to provide a comprehensive overview of the public health principles of mental and neurological disorders This vast range of health conditions affects people across the life course from developmental disabilities in childhood to schizophrenia and substance abuse in adults and dementia in old age Despite this diversity they all share many features they are mostly mediated through brain dysfunction or abnormalities are often chronic in course typically benefit from multi component interventions and are amongst the most neglected conditions in global health The volume will bring together chapters from the Psychiatry Neurology Substance Abuse and Child Development sections of the Encyclopedia of Public Health The volume will be the first comprehensive text on a public health approach to this diverse group of health conditions and has no obvious competitor Highlights the common features of many mental and neurological disorders Provides insights into potential cross over methods of identification and treatment Includes chapters on the most frequently diagnosed mental and neurological challenges faced by public health systems

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