edited by four eminent human geneticists from Johns Hopkins. The book, published in 1988 but almost certainly written in 1986–1987, consists of ten chapters. The editors have chosen the contributing authors well, and many are among the best-known workers at the interface of molecular genetics and medicine. Unfortunately for the interested but uninitiated, however, this book was not written for the novice. Although it is true that several of the chapters (most notably, the introduction and a particularly interesting chapter entitled “Recombinant DNA Analysis of Multifactorial Disease”) are written for a nonacademic audience, the authors of the core chapters of the book, which deal with recombinant DNA methods, clinical application of gene mapping, prenatal diagnosis, and gene therapy, have written as if they were reviewing their area for colleagues or students rather than for newcomers to the field. The instruction of complete newcomers, who might be mildly anxious about their entry into this strange “high tech” world, does not seem to have been uppermost in the authors’ minds. Rather, the chapters seem to be oriented for a first-year graduate student or genetics fellow who already has at least a passing familiarity with the key concepts. This approach is particularly evident in the use of illustrations, which are often inadequately integrated into the text. If the goal is to make molecular genetics nontechnical to the newcomer, this book suffers by comparison with the excellent but now increasingly outdated work of Watson et al. (2). The explanations of linkage analysis do not approach the clarity achieved by Suarez and Cox in a recent pair of articles aimed for a psychiatric audience (3, 4). Furthermore, there is no glossary in this book, and terms such as “allelic,” “exon,” “intronic,” “hybridized,” and “intragenic” are used without definition.

Finally, the book suffers from a common weakness of multi-authored books: repetition. Three different chapters outline the principles of linkage analysis in man, and two review the methodology of Southern blotting. Although repetition can be helpful, in this context the reader would have been better served by an editorial effort to produce one, more thorough explanation of these key concepts rather than the numerous, less adequate ones produced here.

For these reasons, this book will be of most use for those who, although not newcomers to the field of molecular biology, need a refresh and update their knowledge. For such individuals, the book should succeed reasonably well, provided they read it soon, because it will quickly become outdated. Few of the references cited were published after 1986, and the technology in this area is advancing rapidly. For those in the field of mental health, this book is most useful for the insights it provides into the genetics of better understood conditions. Although many may be aware of the problem of allelic heterogeneity (where similar or identical syndromes result from different mutations in the same gene), the magnitude of this phenomenon is strikingly demonstrated by the discussion in chapter three on the genetics of thalassemia. The molecular genetics of this disorder are not almost completely understood, and it has been shown that a similar syndrome can be caused by literally dozens of different mutations. Similarly, genetic heterogeneity (genes at different locations causing the same illness) is currently much discussed in psychiatric genetics. Chapter four provides several clear-cut examples of genetic heterogeneity in well-understood disorders recently revealed by linkage studies.

With enough interest to finish this book will, I suspect, be left with a mixture of awe and envy. As a psychiatric researcher whose work increasingly borders on the field of molecular genetics, I know how the tortoise felt as he watched the hare streak by.

REFERENCES


KENNETH S. KENDLER, M.D.
Richmond, Va.


This is a compilation of results presented at the fifth annual genetic analysis workshop, held at Chantilly, France, Sept. 1–5, 1987. Data sets (real or simulated) concerning human diseases of genetic etiology are distributed at these annual meetings. At the workshop, participants present results of either theoretical developments that would be useful in analyzing such data sets or actual analyses. By agreeing to work on common data sets, the researchers can compare results of different methods of analysis. These papers also appeared in the journal Genetic Epidemiology.

This book is important reading for students of psychiatric genetics. One reason for this is the data sets: the NIMH Collaborative Program on the Psychobiology of Depression—Clinical data set, collected by investigators at five university medical centers and containing families of bipolar probands; the NIMH Family Study, led by Gershon, containing families of probands with bipolar or severe affective disorders; a set of bipolar illness pedigrees informative for X linkage that were reported in different publications; data on human lymphocyte antigen (HLA) typing for bipolar and unipolar families collected in Toronto and in Rochester, N.Y., by Stancer and Weikamp et al.; and five published Old Order Amish pedigrees collected by_Egeland et al., showing strong evidence of linkage to chromosome 11 for bipolar affective disorder.

A focus of the analytic approaches in this volume is the accommodation of genetic heterogeneity. Such heterogeneity can occur in numerous ways. Elston and George discuss inclusion of covariates that may affect familial risk analysis. Family data, based on logistic regression-type models appropriate for family data. One section is devoted to Bonney’s other regression models, incorporated in user-friendly genetic analysis software being developed under Elston’s direction.

Another section of the book concerns segregation analysis and related materials, in which the goal is to build a mathematical model that fits the transmission of (usually) a single trait in nuclear families or pedigrees. The modeling may be based on the Mendelian segregation of a single gene, the assortment of polygenic factors in the family, or random or systematic environmental factors such as sibship environment (the chapters by Demenais and Abel and by Hopper).
Extrafamilial sources of influence such as cohort and period effects can also be incorporated, as shown by Gilligan and Rice in an analysis of the NIMH Family Study data. The papers concerning linkage relationships between affective disorder and specific genetic markers are, perhaps, the centerpiece of the book. Martinez et al. discuss the effects on linkage analysis of misclassification of affective disorder in relatives, and Greenberg and Hodge take up the effects on linkage analysis of the intrusion of a second gene that affects the penetrance of a first gene (epistasis). A three-allele model to account for the fact that bipolar and unipolar affective disorders occur in the same family is proposed, fit, and tested by Sandkühl and Ott. Van Eerdegeweg offers modifications of existing linkage programs to take account of cohort effects and of large, highly inbred pedigree structures. (Older linkage programs could deal with inbreeding either not at all or only in small quantities. In groups such as the Old Order Amish there is a lot of inbreeding, and this can strongly affect the results of linkage analysis under certain circumstances.) A relatively efficient, inexpensive method of screening for linkage is the affected sib-pair method, and Chakarovaiby discusses using this method to detect linkage of sex-linked dominant diseases. Wilson argues against the conventional habit of using peak lod scores as the sole summary statistic for deciding whether there is evidence for linkage. She suggests a Bayesian approach that takes into account the whole lod curve. Finally, the controversial issue of HLA and affective disorders is taken up in three papers that do not achieve a convergence of results. Weitkamp and Stancer’s suggestion suggests that there is an HLA-linked gene for susceptibility to affective disorder, whereas Price finds the opposite. I find the case more convincing on the negative side.

This is a complex book, parts of which are mathematically rather sophisticated. The editing shows few lapses. There is a missing leading term in the second equation on page 58, and there are several small errors in the chapter by Hopper (e.g., equation 31 on page 237). Although these do not detract from the readability of the manuscript for those familiar with mathematical models, it is a pity they crept into a book that might be read by nonspecialists.

Genetic analyses, in particular linkage analyses, are going to become more important in psychiatric research over the next few years. This volume is a good, up-to-date account of some of the more recent methodological advances that have been made in human genetic modeling. The importance of the progress being made is that complex phenotypes like psychiatric disorders require complex models. Environmental effects, cohort effects, effects of age at onset, familial heterogeneity in disease manifestations, and very likely genetic heterogeneity between the sources of genetic variability from one family to another all plague the analysis of psychiatric family data. Hitherto, analysts have mostly had to ignore the complications, because the available analytic methods were not up to dealing with them. We can look forward to a future in which data will not have to be forced into models in a Procrustean fashion but, instead, more or less satisfactorily incorporated. I recommend this volume to readers who need an introduction to the current state of knowledge in genetic statistics related to psychiatric family data.

WILLIAM M. GROVE, PH.D.
Minneapolis, Minn.

Reprints of Book Forum reviews are not available.

NEUROPEPTIDES


The time between a neuropeptide’s discovery and its implication in disease states is usually brief, which, along with the exponential rate at which new neuropeptides are being defined, guarantees that clinical research findings involving this class of neurotransmitters will continue to proliferate. However, since the early stages of any novel research enterprise are often dogged by methodological issues and questions of reproducibility, many early “neuropeptide” findings will almost certainly be amended or refuted. To present a critical yet coherent perspective of such a changing body of data is a formidable enterprise for any editor. Dr. Nemeroff has acquitted himself admirably. He and his distinguished contributors have produced an edited collection that is neither repetitive nor discontinuous and is eminently understandable to anyone with an interest in clinical neuroscience.

One might be advised to approach Neuropeptides in Psychiatric and Neurologic Disorders by reading the last chapter first. In it Dr. Widerlov offers a welcome overview of the establishment of neuropeptides as bona fide neurotransmitters and provides an outline of the other chapters. The collection delivers what it promises. Apart from a review of the peptidergic neuron, the subject matter is oriented to human disease states. A general discussion of neuropeptides as diagnostic research tools is followed by a series of chapters each devoted to a specific pathophysiological condition. These include schizophrenia, manic-depressive illness, dementia, Huntington’s disease, Parkinson’s disease, sleep disorders, and pain. This classification permits authors to cross usual boundaries and present data from a multiplicity of research approaches, ranging from post-mortem neurochemistry to neuropeptide challenge paradigms. Given the youth of this research area, the reader should not be surprised that authors have drawn generously from basic sciences and may devote a good deal of effort to discussions of confounding factors while presenting often disparate results from their own and their colleagues’ work. Although those new to neuropsychiatric research may wish for less hypostatizing and more dogma, the authors must be commended for avoiding overgeneralized interpretation.

Since neuropeptides are not used as routine clinical diagnostic or treatment tools at present, this edited collection will find its greatest favor with two groups—those researchers interested in clinical implications of neuropeptides in general and those investigators in psychiatry and neurology who want to know how neuropeptides might be involved in a specific clinical state. Dr. Nemeroff and his collaborators have provided the best and most comprehensive reference on neuropeptides in neuropsychiatric available to date. The rapid developments in their field demand a sequel.

GEORGE E. JASKIW, M.D.
Washington, D.C.

Ritual Abuse

SIR:

As the our kr sant e

N pers apy fear and her ing:

Ms. mg dect emp

She der her with caus 1 m

mon pear she por exch

Alth though is of f pose. is unphysio deed, f and an a place illicit c eding a patien t an act possibi thymia

Beca