BOOK REVIEW

Mood Genes: Hunting for the Origins of Mania and Depression

by Samuel H. Barondes
1998 Oxford University Press 237 pages

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In ***Mood Genes*** Samuel Barondes uses a very readable format to recount progress toward understanding the molecular basis of bipolar disorder. The chapters range from autobiographical accounts of Dr. Barondes' involvement in this quest, to biographical sketches of important players from Freud and Kraeplin through Mendel and Morgan to Housman and Escamilla and a healthy dose of genetics instruction. The veritable who's who of psychiatry, classical and molecular genetics is presented with two well-delivered underlying themes: the first is the life of 'Michael', a scientist whose family history of bipolar disease leads to concerns for his children, and the second, the basic science that underscores every advance in the quest.

I read the book as background for a case study used in my upper level Cell Biology course. Although I did not assign any readings from ***Mood Genes,*** I may in the future. During class I referred to its contents often and even read aloud passages including a discussion of how mutations are not just 'bad' or 'good', their effects are determined by the environment and circumstances and quotations from Kay Redfield Jamison on the 'up-side' of having bipolar disorder. The prose is very accessible and appropriate for sophomore through senior undergraduates in psychology, neuroscience, and biology. First year students and non-majors may stumble a little on the science but should find the book's delivery and outlook within their level.

The first chapter sets up the topic and introduces the reader to how a chance roommate assignment to 'Michael' at a 1970s workshop piqued Barondes interest in bipolar disorder. Michael's family helps to tie the book together as later interactions between Barondes and Michael and references to how developments would apply to Michael give the scientific facts an immediate human face.

The second through fourth chapters include developments in psychiatry and biology that occurred prior to Michael and Barondes' meeting. Early views of mental illness and the categories currently used to describe varying degrees of affective disorders are discussed. These chapters also provide the initial examples of how the personal story and the scientific one will be intertwined. Alkaptonuria (AKU, a rare form of arthritis), Alzeheimer's disease, and syphilis are used as examples to illustrate both how scientists approach those diseases and how such approaches were inadequate in the search for the cause of bipolar disorder.

In the third through the eight chapters, Barondes provides a lucid course in Mendelian and molecular genetics without ever sounding 'textbook-ish'. Emil Kraeplin's concept of mood disorders as a result of "hereditary taint" leads smoothly into a discussion of the circumstances causing an Augustinian monk to spend time analyzing the offspring of pea plants. Students may find these circumstances interesting because Mendel, the father of genetics, started on this project as part of remedial training. He had failed his teaching certificate examinations.

Because multiple genes are likely to be at the root of bipolar disorder the genetics explained in ***Mood Genes*** necessarily goes beyond the concepts of recessive and dominant traits. After providing the basics through straight-forward inheritance examples, like AKU and Huntington's disease, the more difficult cases are tackled. The symptoms of King George III (porphyria) and Abraham Lincoln (Marfan's syndrome) are used to explain penetrance and expressivity clearly. These descriptions and analogies are worth reading if you are searching for ways to explain genetics to an introductory class or to a layperson. Barondes is also careful to point out that the diagnosis of King George III and Lincoln are posthumous and controversial. The fact that the actions and stature of these men are so well known allows the reader to form a mental image of the disorders quickly even if using them as examples of porphyria and Marfan's syndrome does border closely on propagating an 'urban legend'.

The genetics then progresses from Mendelian to molecular and the search for chromosomal locations of mood genes. Again the approach is to build from straight forward examples to more complex ones. The discovery of the mutation in hemoglobin that causes Sickle Cell Anemia by Pauling, Itano, and Ingram, to the work of Morgan and his studies of genetic linkage are explained. Through this Barondes also discusses societal changes from approaching research as a hobby of gentleman or monks to a profession concerned with laboratories, more advanced equipment and many collaborations.

Linkage mapping through Restriction Fragment Length Polymorphisms (RFLPs) is broached both in scientific context and as an important research tool. Barondes relates how Botstein, White, Skolnick, and Davis proposed RFLP mapping and the value of molecular markers. As someone who includes RFLP analysis in my introductory biology course, I found his description of RFLPs and SNPs very clear and an approach I can adapt for my own lectures.

The application of RFLP analysis is shown through Gusella and Conneally's mapping Huntington's disease to the tip of Chromosome 4. Like the discovery of the cause of Sickle Cell disease, this example is one used in other texts. In this book, as others, the examples do a good job

of underscoring the techniques used. Barondes' book, however, also points out the historical perspective of events surrounding this work and the fact that the study included both good science and good luck.

Barondes discussion mood gene mapping attempts reveal that Bipolar Disorder is neither straight forward no does it suffer from an excess of good luck. In some ways the disorder is a reflection of the way research progresses. The history includes glimpses of elation and exuberance balanced by serious setbacks and gives a view of research that would supplement the linear 'hindsight' often seen in textbooks. Barondes discusses the personal aspects; families not wanting to be involved in pedigrees for fear of societal repercussions, researchers searching for funds, and the role of time and timing.

These kinds of stories around the science are seen throughout the book. They include Barondes continuing narrative of how he became involved, the discussions, over Sacher-tortes, dinner, or drinks, that shaped the direction of his career, and later, shaped his views on funding panels. They also show that while science builds, sometimes the building is on discoveries from other fields and sometimes it is on the ashes of a once-loved hypothesis.

The examples, especially AKU and Alzheimer's disease, become part of a foundation of facts to which Barondes refers throughout the book. The style of writing allows the reader, in later chapters, to feel the progression and see how current work builds on the shoulders of previous discoveries. Through explaining the web-like progression of scientific study and the tie to Michael, Barondes tells a scientific story that is true to the science and refrains from becoming schmaltzy or maudlin. The book remains authentic and the way all of the examples come together is either masterful planning or great serendipity.

The book ends with important public service information. This includes characteristics that may indicate someone is suffering from bipolar disorder and a discussion of the benefits and costs of developing a test for people predisposed for the disease. An interesting development in this arena was published recently by Sklar et al. (2002). This research has identified single nucleotide polymorphisms (SNPs) in the growth factor brain-derived neurotrophin (BDNF) that may be risk indicators for bipolar disorder. The researchers are thorough in their analysis but caution that larger studies need to be performed before the public health significance of their findings can be truly assessed. This study underscores, however, that discussions over testing may need to happen sooner rather than later. Barondes' book was written well before these developments but his information about false starts does provide a backdrop for the cautious nature of Sklar and colleagues announcement. Another note is that ***Mood Genes*** was published as the field of genomics began and therefore only briefly touches on the potential of microarray analyses to identify the genetic basis of mood disorders.

One criticism of the book lies with its somewhat lax use of in-text references. It contains a helpful index but no footnotes or endnotes are indicated anywhere in the text. Since students often find the many footnotes of journal article disruptive the removal of superscripts may make it easier for them to read the book, but references are important so that proper credit is given. Most textbooks also omit the use of footnotes but, in those cases, the references are found at the end of each chapter. I read the book all the way through before realizing that any endnotes were provided. When I did read them I found that they contained other explanations that were quite useful.

Overall ***Mood Genes: Hunting for the Origins of Mania and Depression*** is very well written. It 'reads easily' and would be a good supplement to more traditional textbooks for classes that focus on the genetics of mood disorders or other inheritable diseases.

REFERENCE

Sklar P, Gabriel SB, McInnis MG, Bennett P, Lim YM, Tsan G, Schaffner S, Kirov G, Jones I, Owen M, Craddock N, DePaulo JR, Lander ES (2002) Family-based association study of 76 candidate genes in bipolar disorder: BDNF is a potential risk locus. Mol Psychiatry 7:579-593.