Polarized Perspectives: Environmental and Genetic Causes of Bipolar Disorder

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Abby* races violently around her artistically decorated dorm room. Flinging framed pictures of her now ex-boyfriend against gray walls, she cries hysterically. She takes a handful of anti-depressants and swallows them one after the other in defiance. They fail to fill the void. She lies on brown carpeting, staring at a speckled ceiling and wondering why she’s such a mess. She can’t control anything anymore—not even her own irrational actions. Alone with her rapidly spiraling mind, Abby faces a struggle she can’t define. She is not just another heartbroken girl or case of anxiety and depression. Abby faces another kind of mysterious and misunderstood psychological disorder.

This short scene tells the story of my closest high school friend and her struggle with bipolar disorder. Diagnosed after a manic episode of unhealthy pill popping and screaming desperation, Abby has learned to live with the disorder. Witnessing Abby’s experience, I asked a question that scientists and researchers are continually pondering and examining: What causes bipolar disorder? Despite its strictly defined subtypes and symptoms, the exact cause of the disorder remains undefined. Studied rigorously over the past three decades, the disorder remains mysterious in its origins, and a definite cure is elusive. This paper explores a small sample of specific experiments and theories from 1970 through 2010 that present varying perspectives about the causation of bipolar disorder—moving from theories of environmental influence, to the genetic linkage of bipolar disorder to several different chromosomes.

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Bipolar disorder is a long-term psychological condition known to create extreme fluctuations in mood—ranging from lows of depression to extreme manic highs. The rate of mood swings varies from many times a day to a handful of episodes in a year. The condition can be controlled with the use of medication and counseling. The disorder is defined in a hierarchy of severity. There are three different levels of bipolar disorder: Bipolar I disorder, Bipolar II disorder, and Cyclothymia. Bipolar I involves intense and potentially dangerous manic episodes, and often negatively impacts work, education, and personal relationships. Bipolar II is not as severe as Bipolar I, but still includes heightened mood and agitation. It is possible to live a more normal everyday life with this level of the disorder. Finally, Cyclothymia is the mildest form of the disorder, with generally less severe psychological highs and lows (Mayo Clinic Staff, 2010, p. 1).

Generally, the manic stages of the cyclical bipolar disorder include symptoms of “extreme optimism, poor judgment, inflated self-esteem, racing thoughts, decreased need for sleep, increased sex drive, [and] careless or dangerous use of drugs or alcohol” (Mayo Clinic Staff, 2010, p.2). The depressive stages of bipolar disorder include symptoms of “sadness, hopelessness, suicidal thoughts or behavior, anxiety, guilt, sleep problems, loss of interest in daily activities, irritability, and poor performance at work or school” (Mayo Clinic, 2010, p.3). Bipolar disorder is also known to cycle with the seasons—manic episodes occurring in either the warmer seasons of spring or summer and depression occurring in the fall or winter. The reverse can also be true. The mood shifts may also be rapid, involving more than four mood swings in one year, or even within a series of hours. Overall, bipolar disorder and its ramifications vary from person to person, and
remain largely unpredictable. This makes the search for its cause and eventual cure all the more difficult and urgent.

Furthermore, bipolar disorder often goes undiagnosed and untreated. Those with bipolar disorder often enjoy the highs of the cyclical nature of the disease, and feel detached from their true selves and personalities when medicated. The most noticeable symptoms in children and teenagers include “explosive temper, rapid mood shifts, reckless behavior, and aggression” (Mayo Clinic Staff, 2010, p. 4).

When it comes to causation, these several possible explanations reflect the uncertainty of the medical and scientific communities. The first explanation offered is biological differences—described as physical differences in brains of those with bipolar disorder. An imbalance in neurotransmitters and hormones is also linked to the disorder. Finally, inherited traits and environment are emphasized as probable influences on the onset of bipolar disorder. With bipolar disorder more often diagnosed in people with a family history, and links between the disorder and surroundings of stress, abuse, and trauma, the ongoing study of genetic and environmental influence in bipolar disorder is the exploratory focus of this research paper.

**Bipolar Disorder and Environment**

In a chapter focused on pediatric bipolar disorder in the *Handbook of Adolescent Behavioral Problems*, a portrait of an adolescent suffering from bipolar disorder and its symptomatic poor judgment and risk taking is described. This individual is painted as a “younger [who] call[s] 1-900 sex lines, suddenly start[s] dressing inappropriately…masturbate[s] excessively…simulate[s] sexual activity with animals…or pressure[s] parents to buy expensive/inappropriate clothing” (Pavuluri,
Naylor, Sweeney, 2005, p.187). Though this is an extreme portrayal, it is one that makes it very easy to associate behavior with environment. Reading about a teenager obsessed with sex, masturbation, and other degrees of inappropriate sexual expression, the immediate questions that come to mind pertain to what sort of parenting environment this child is exposed to, and why and how they have “learned” the behavior. Later in the article, this initial assumption of a link between inappropriate behavior and outside stimuli or damaging experiences is acknowledged. However, data reveals an interesting complexity as the article states: “a history of sexual abuse is often considered in differential diagnosis in these poorly socialized, sexually disinhibited children. In an ongoing phenomenological study, only 1.1% of the [bipolar disorder] sample had a history of sexual abuse or over stimulation, while 43% exhibited hypersexuality…supporting hypersexuality as a critical symptom in [bipolar disorder]” (Pavuluri et al., 2005, p.187). Of course, hypersexuality is a disorder that does not have a clear cause (environmental or genetic) (Solovitch, 2010, para.2). Therefore, although hypersexuality has been isolated as a telling symptom of bipolar disorder, it is still unclear how environment influences its development.

Despite this puzzling and circuitous data, Pavuluri, Naylor, and Sweeney go on to acknowledge the social and community factors of bipolar disorder. Connecting the influence of American culture and the increased use of medications to high rates of bipolar disorder, these authors state: “one of the reasons offered for the higher incidence in the USA was the increased prescription of stimulants and antidepressants that are likely to precipitate a predisposed condition” (Pavuluri et al., 2005, p. 190). Because the impact of culture is almost impossible to measure, this statement is not backed up by
specific data, but its inferences are intriguing. In a country quick to write prescriptions, perhaps those who have the genetic predisposition for bipolarity (i.e. it is found in their family tree) could find the disorder expressed more fully due to their use of anti-depressant medication.

Beyond the impacts of a pill popping American culture, Mani N. Pavuluri et al. also explore the success of the positive influence of family and community upon living with bipolar disorder. This treatment is entitled *Psychosocial Therapy*. The treatment method involves “psychoeducation, family problem-solving, improving communication…managing crises, and helping the patient rehearse and develop coping strategies in the event of future relapse” (Pavuluri et al., 2005, p. 197). Though these strategies make intuitive sense, addressing the potential healing effect of a positive environment, they are not proven. Again, as with culture, it must be acknowledged that the influence of family and community is incredibly difficult to measure. However, this does not mean that the impact is unimportant. For example, “Geller et al. (2002) reported that more than half of those diagnosed with [bipolar disorder] had no friends, were teased by other children, and had poor social skills…there was a high degree of hostility and low warmth in maternal-child relationships, poor agreement between parents on child-rearing practices, and minimal problem-solving skills” (Pavuluri et al., 2005, pp. 1890-90).

Interpreting this data and observation taken from people already diagnosed with bipolar disorder, it makes sense that positive manipulation of environment could help to diminish the effects of the disorder. Furthermore, it suggests that a negative environment (involving poor parent-child relationships and exclusive social situations for example) could be a significant factor in the onset of bipolar disorder and its symptoms.
It is important to note that this section of Pavuluri, Naylor, and Sweeney’s data is particularly interesting because it focuses on children with bipolar disorder. Detailed in a chapter titled “Bipolar Disorder” in the book *Childhood Mental Health Disorders: Evidence Base and Contextual Factors for Psychosocial, Psychopharmacological, and Combined Interventions*, diagnosing bipolar disorder in children is controversial. The attribution of children’s symptoms to bipolar disorder is debatable because irritability is linked to many other childhood disorders, and many children exhibit behavior that could be defined as manic—generally falling into the category of extreme mood swings (Brown et al., 2008, p. 87). The National Institute of Mental Health expands on this debate as they state: “Children with a parent or sibling who has bipolar disorder are four to six times more likely to develop the illness, compared with children who do not have a family history of bipolar disorder. However, most children with a family history of bipolar disorder will not develop the illness” (National Institute of Mental Health [NIMH], 2009, para.1). This statement suggests that there must be some other sort of underlying cause of bipolar disorder that does not deal directly with family hereditary lines—paving the way for environmental influence.

In an article entitled “Tracking Down the Footprints of Bipolar Disorder,” it is emphasized that bipolar disorder is generally revealed and diagnosed in adolescent years—particularly in women. A subheading is also dedicated to childhood-onset bipolar disorder. This is a new form of the disorder that is currently diagnosed at younger and younger ages. Phillips admits that bipolar disorder is more problematic to diagnose in children than in adults because it overlaps with so many other childhood behavioral issues.
Furthermore, Phillips offers potential links between childhood bipolar disorder, bipolar disorder in general, and the environment. She points out that certain cases may develop due to hormones, stress, or pesticide exposure. Interestingly, Phillips hypothesizes that because our current culture has fostered rampant childhood obesity and diabetes, sugar metabolism may play a role in bipolar disorder—tying into Pavuluri et al.’s notion that culture can influence the disorder. Moving further with this idea, Phillips outlines the projections of specific cultural practices, including diet, onto the onset of bipolar disorder. Phillips implies that standardization could help to identify and eliminate certain environmental factors from the list of causes. She offers the example that the Japanese are known to have significantly lower occurrences of depression than Americans, stating: “This is because Japanese have a higher intake of omega-3 fatty acids from eating more fish. Now some psychiatrists are using omega-3 fatty acid supplements to help control depressive symptoms in their bipolar patients” (Phillips, 2005, para. 3). She uses this information to infer that if country-by-country studies were conducted, the role of hormones in bipolar disorder could be determined and addressed in each country—acknowledging that varying cultures have different diets and consequently different chemical exposure and hormone levels that could demand specialized treatment (Phillips, 2005).

Examining the input of Pavuluri, Naylor, Sweeney, Phillips, and several other background sources, the role environment plays in the onset of bipolar disorder is revealed as ambiguous, yet impossible to ignore. Difficult to measure or to prove, Environmental factors continue to be a perplexing element in the study of causation of bipolar disorder. Despite the logical attribution of environmental factors to the onset and
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severity of bipolar disorder, many psychologists present a strong case for genetic influence in bipolar disorder—tracing family trees and isolating genes and chromosomes in hopes of discovering a provable and reliable cure.

1972 X Chromosome Linkage

In a study from the early 1970s emblematic of the tantalizing search for a specific genetic cause for bipolar disorder, Ronald Fieve and Joseph Fleiss of the New York State Psychiatric Institute and Julien Mendlewicz of the University of Brussels conducted extensive research to prove a link between bipolar disorder and the X chromosome. Their study evaluated 80 bipolar patients, and found “a linkage association in seven families who had both the color-blind marker and the manic depressive illness” (Society for Science & the Public, 1972, p. 134). The evidence cited in the study was revolutionary and seemed definite, but in the end could not be deemed the universal cause of bipolar disorder. As Fieve is quoted in the Society for Science & the Public journal: “the evidence is…convincing…but it does not mean that all cases of manic-depressive illness are transmitted by the X-linked gene” (Society for Science & the Public, 1972, p. 134). Fieve modeled his study after the study of other psychological disorders—attempting to link bipolar disorder studies to studies of patients suffering from depression and schizophrenia. If his studies were effectively carried out and conclusive, genetic linkages among psychological disorders could be determined and chromosomes affecting the diseases could be isolated—opening a venue for their manipulation and suppression of the expression of psychological disorders. Noble and ambitious in his goals, Fieve believed that genetic types of psychological disorders like schizophrenia could be separated from non-genetic types. Fieve built his unparalleled research on the idea that
genetic influence can be separated from the impact of environment. Whether or not this is the case, his studies opened a door in the search for a cause for bipolar disorder, and represented one door-opening facet of an intricate network of genetic studies on the subject.

**1989 Disproval of Chromosome 11 Theory**

A beauty and curse of the nature of science, compelling theories and studies are often contradicted and rendered useless—sending years of hard work and hopeful conclusions back to square one. Such was the case in the 1989 discovery made by John Kelsoe, a psychiatrist collaborating with the National Institute of Mental Health and the National Cancer Institute. Initially attempting only to confirm a 1987 study of an Amish population by Janice Egeland of the University of Miami that isolated the cause of bipolar disorder as a mutation found on chromosome 11, Kelsoe instead located a fatal development. Egeland had carried out a genetic analysis of the inheritance of bipolar disorder in an Amish family—ideal due to its large size and easily traced gene pool. Her study found a dominant gene through statistical analysis, and used linkage analysis to determine that the influence came from the tip of chromosome 11. Trying to recreate Egeland’s study, Kelsoe returned to the family lines of the Amish family from the study. As he examined 40 subjects who were not in the original study, he found that one was diagnosed with bipolar disorder, but did not have the DNA marker on chromosome 11 that Egeland defined as necessary for the disorder to occur. He also found that a new branch linked to the original family by marriage had a form of bipolar disorder, but it was not linked to chromosome 11 (Barinaga, 1989, p. 886). These subtle discoveries were enough to discredit Egeland’s hope-inspiring theory—demonstrating the importance of
re-checking studies and the difficulty of truly isolating *one* genetic cause for a disorder. This process is emphasized in an article entitled “Manic Depression Gene Put in Limbo” from the journal *Science*, as author Marcia Barinaga states: “Along the way to their surprising conclusion, all the researchers involved learned some…sobering lessons about the pitfalls of doing genetic analyses of illnesses as complex as manic depression—lessons that may apply equally well to other illnesses” (Barinaga, 1989, p. 886). In a complex world of circular connections and the influence of countless tangled interactions, Barinaga makes a good point that probes the question: is a search for *one* genetic cause of bipolar disorder ultimately futile?

**Multiple Genetic Markers**

Embracing the theory that genetic causation is likely interactional and not traced to one specific point, a 1996 article entitled “Manic-Depression Findings Spark Polarized Debate” written by Virginia Morell for the journal *Science* explored three studies representative of the debate between support of multiple and sole genetic causes of bipolar disorder (formerly called manic depression). One study found several potentially influential loci, a second found evidence for a single marker on chromosome 4, and a third was a multigenic study that followed an Old Order Amish family. Instead of isolating just one chromosome as Egeland did, the multigenic study found evidence of bipolar disorder on chromosomes 6, 13, and 15. The influence and interactions of several chromosomes and a multigenic outlook pervaded the thought-provoking article. Neil Risch, a geneticist at Stanford University in 1996, summed up the stance of the paper in one biting quotation, stating: “We have four genes for Alzheimer’s, two for breast cancer, yet not one for manic depression despite all of these intensive searches. Why is that?
Now we have five more loci being claimed to harbor genes. Given the past history of the field, it’s not clear to me which if any of these is real”(Morell, 1996, p. 32). Risch uses divergent genetic results to make a solid point that truly and completely solving the mystery of causation for a disorder is a nearly impossible feat. There will always be epistatic effects—interactions between chromosomes, genes, and potentially the outside environment—knotted together and requiring decades to unwind.

**Bipolar Disorder and CLOCK**

In a more recent study that took place in 2007 and was reported in the *Proceedings of the National Academy of Sciences of the United States of America* journal, researchers determined that the central transcriptional activator of molecular rhythms, otherwise known as CLOCK, plays an important role in bipolar disorder. By studying mice that carried a mutation in the CLOCK gene, (which is known to be associated with circadian functions like sleep, activity, and appetite that are disrupted in bipolar disorder), researchers found that the mice behaved incredibly similarly to humans with bipolar disorder—demonstrating symptoms of “hyperactivity, decreased sleep… and an increase in the reward value for cocaine” (Roybal et al., 2007, p. 6406). Giving the mice lithium (a mood stabilizer) helped the mice to return to more “normal” behavior—suggesting that the same lithium administration could be effective in humans. The study also made the important discovery that CLOCK plays a strong role in the regulation of behavior and mood. This examination of CLOCK served to isolate a specific subset of genes that undoubtedly play a part in bipolar disorder (particularly its cyclical and seasonal nature.) However, as was true with several of the studies discussed previously, the results are not air-tight. In the discussion section of the article entitled “Mania-Like Behavior Induced
by Disruption of CLOCK” in Proceedings of the National Academy of Sciences of the United States of America, the vastness of what remains unexplored in the realm of CLOCK’s impact is expressed. Hinting at the overlap of environmental and genetic influences, the article states: “future studies are needed to determine whether depression-like symptoms occur in these mice after periods of stress, activity, or sleep deprivation…future experiments will determine which genes are direct transcriptional targets of CLOCK… and how they are involved in regulating dopaminergic activity and manic-like behavior”(Roybal et al., 2007, p. 6409). This study must be replicated and the results confirmed in order to remain credible, and it must be expanded to explore external environmental factors of stress and sleep. As the study of bipolar disorder continues in mice, it seems that holistic conclusions should be drawn that cover both environmental and genetic variables in order to more fully understand the human condition of bipolar disorder.

Conclusions

Evaluating research from both sides of the debate about the cause of bipolar disorder, the cases for environmental and genetic influence each resonate in different ways. As is reported by the National Institute of Mental Health in an overview of the disorder, “people who have a parent or sibling with bipolar disorder are four to six times more likely to develop the disorder than people without family members who have it” (NIMH, 2009, para. 2). This connection of bipolar disorder to genetics and inheritance is impossible to overlook. The genetic studies summarized in this article are groundbreaking and progressive—illuminating the influence of family history and
genetic predispositions to come closer to a cure. Perhaps most promising are those that begin to examine *multiple* chromosomes and incorporate influences outside of genetics. This was true in both the multiple genetic markers study and the CLOCK study. Though the specificity of genetic studies is beneficial, it is also limiting. For example, in an article written for livestrong.com that gives an overview of bipolar disorder, it is revealed that *most* people who have a family history of bipolar disorder never actually develop it (Butler, 2010). This infers that genes may predispose bipolar diagnosis, but that environmental triggers play a role in the disorder’s emergence. Following this logic, Jennifer Phillips stresses the partial impact of environment in her article “Tracking Down the Footprints of Bipolar Disorder” as she discusses an identical twin study done on bipolar disorder. Because identical twins share 100% of their genetic information, if genetics were the sole cause of bipolar disorder, then in every case of one identical twin having bipolar disorder the other would also be diagnosed. However, Phillips states: “various studies show that identical twins have a concordance of only 28.96%” (Phillips, 2005, para.1). Again, the weight of the environment cannot be brushed aside. Ideally, future studies pertaining to the causation of bipolar disorder will incorporate both environmental and genetic variables—preferably across several genes. Despite the vastness and complexity of this endeavor, there are already steps being made in the right direction to make it possible. For example, Phillips addresses the tracking of genes through a method called “gene expression” that has developed in the last decade (Phillips, 2005). This process of testing thousands of genes simultaneously was previously used in cancer research, and can be used to differentiate bipolar disorder from forms of schizophrenia and detect “molecular abnormalities” in bipolar people (Phillips, 2005).
Using this efficient method of genetic study in conjunction with studies of environmental influence could prove effective in ultimately determining the causes of bipolar disorder.
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