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Bipolar Disorder: Causes, Effects, and Possibilities

One of the world's most common, severe, and persistent mental illnesses, bipolar disorder is a neurological condition that alters a person's capacity to experience a normal range of moods. As the name suggests, the disorder is characterized by two alternating poles in behavior—mania and depression—which express themselves in four types of episodes—manic, hypomanic, depressive, and mixed—each lasting a week or more in duration.

At the onslaught of a manic episode, a sufferer of bipolar disorder may experience a burst of energy, creativity, and sociability; this emotional “high” is tempered by irritability and denials of any change in behavior. The sufferer may then experience any of the following symptoms: insomnia; inflated self-esteem; talkativeness; flight of thoughts; distractibility; more goal-oriented activity; psychomotor agitation; indulgence in hedonistic and reckless behaviors (i.e. sexual indiscretion); and, in severe cases, visual and auditory hallucinations. These symptoms must last for at least one week in order to constitute a manic episode; they may damage a patient's ability to function normally in the workplace and in relations, creating patterns of very poor judgment which can damage a person's finances, career, and reputation. This form of self-destructive mania may require containment and family support. Hypomanic episodes involve

similar but less severe symptoms, which last only four days; they do not include psychotic episodes or major impairment of functionality in quotidian life for the patient.

At the other extreme, depression can have an even more detrimental impact on the ability of a sufferer to function normally, and may create the necessity for commitment or hospitalization. Depressive episodes are characterized by the following symptoms, which last at least two weeks: depressed mood; diminished interest or pleasure in daily activities; weight loss or decrease of appetite; insomnia or hypersomnia; psychomotor agitation or retardation; fatigue; feelings of worthlessness or guilt; diminished ability to think, concentrate or make decisions; and recurrent thoughts of death.

Mixed episodes involve alternation between the symptoms of mania and depression, and can be more disabling, and pose greater risk of suicide than either.¹ Suicide is generally considered the greatest danger associated with the depressive phase, and the threat it poses is life-long. Other major dangers of bipolar disorder include homicide and other violent behaviors, often associated with the manic phase, when the sufferer may become grandiose and exigent around others; and addiction, which poses the unique problem of establishing a dual diagnosis and complicating treatment possibilities. Bipolar disorder has a significant morbidity and mortality rate: between 25-50% of sufferers attempt suicide, and 11% are successful.

¹ American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders. 4th Ed. Text Revision.* Washington, DC: American Psychiatric Association; 2000.

Bipolar disorder represents one extreme on a more or less continuous spectrum of mood disorders including bipolar I, bipolar II, cyclothymia (oscillating high and low moods), and major (unipolar) depression. Bipolar I is also referred to as classic manic-depression and is the most severe of these disorders, with the greatest range of extremes in mood. Bipolar II involves the same depressive episodes as bipolar I, but they alternate with hypomanic episodes, rather than manic episodes.²

Bipolar disorder affects communities all over world and has an international frequency of 0.3 to 1.5%. No racial predilection has been found, though in practice clinicians tend to diagnose African and Latin Americans with schizophrenia rather than bipolar or other affective disorders more commonly than they do in treating Caucasians. Bipolar I is equally common between the sexes, but both bipolar II and rapid-cycling bipolar disorder (wherein the patient experiences four or more episodes per year) are both more common in females than in males. The age of onset of bipolar disorder varies greatly, ranging from childhood to 50 years, with a mean age of 21. Most individuals experience the onset of symptoms between the ages of fifteen and nineteen. Sufferers of bipolar may not experience their first manic episode until after the age of 50 but experience depressive episodes in from a younger age, and thus be diagnosed with major depression.³

The etiology and pathophysiology of bipolar disorder are still widely unknown. No objective biological markers definitively indicate the presence of

² Ibid.

³ Soreff, S.M.; McInnes, L. A. *Bipolar Affective Disorder*. Emedicine.com, 2000.

the disease. Studies comparing incidence of bipolar disorder among monozygous (identical) twins and heterozygous (fraternal) twins have been conducted to determine whether the disease might be inherited; these studies have found that indeed, between monozygous twins there is a correlation rate of 57%, while between heterozygous twins there is a correlation rate of 14%.⁴ These studies are continuing and are expected to be aided by new advances in both knowledge and technology developed in the Human Genome Project.

In order to determine whether bipolar disorder was transmitted through imprinting or mitochondrial inheritance, McMahon et al. conducted a study of 31 families wherein one of the parents was affected by the disorder, tracking the frequency among their relatives. They discovered that in cases where the mother was the infected parent, her relatives were at 2.3 to 2.8 times risk of developing the illness. Likewise, the children of couples with an affected mother showed a 1.3 to 2.5 percent higher risk of illness. These findings indicate that the phenotype might be transmitted specifically through mothers.⁵

Several studies of the genetic causes of bipolar disorder have suggested multiple genetic loci, but no specific genes have yet been concretely identified, owing in part to the small effects of many genes on different individuals, and in part to the fact that there yet exists no means of objectively identifying a particular

⁴ Cadoret, R. J. : "Evidence for genetic inheritance of primary affective disorder in adoptees." *Am. J. Psychiat.* 135: 463-466, 1978

⁵ McMahon, F. J.; Stine, O. C.; Meyers, D. A.; Simpson, S. G.; DePaulo, J. R. : "Patterns of maternal transmission in bipolar affective disorder." *Am. J. Hum. Genet.* 56: 1277-1286, 1995.

genetic subtype. The Columbia Bipolar Genetic Study found a possible marker for the disease gene on chromosome 21; these findings have been reproduced. Other studies have found possible makers on chromosomes 4, 13, 18, and the X-chromosome.

Other genetic studies are also being conducted to understand better the pathophysiology of bipolar disorder. Like related depressive disorders, it affects the prefrontal cortex ventral to the genu of the corpus callosum. This area is generally associated with diseases wherein emotional and autonomic symptoms appear in response to external, social stimuli. (It is also the site of the brain containing the neurotransmitter systems affected by anti-depressant drugs.) Positron emission tomography (PET) scans of cerebral blood flow and rate of glucose metabolism show decreasing activity therein, while magnetic resonance imaging (MRI) scans reveal a reduction of the volume of the cortex. It's suggested that bipolar disorder is caused by abnormal programmed cell death (apoptosis) in the parts of human brain circuitry that regulate emotion. If this is the case, mood stabilizers and antidepressants may offer treatment for the disease by recuperating cell survival pathways and supplanting neurotrophic substances that improve cellular resiliency. However, many biochemical pathways are likely involved in the disease, which is why detection of one particular abnormality hasn't yet been achieved.

Several neurotransmitters have been linked to the disorder. Bipolar disorder, like many mood disorders, has been treated with tricyclic and new generation antidepressants, such as Prozac, Selexa, Paxil, and Zoloft; it has also

been treated with monoamine oxidase inhibitor tranylcypromine. Studies of affective disorders have found that certain drugs are more effective for certain families: monoamine oxidase inhibitor tranylcypromine are more successful among families with multiple sufferers of major depression, and lithium treatments are more successful among families with high susceptibility to bipolar disorder. Neither treatment is as effective in families with multiple sufferers of schizophrenia. On the basis of these studies, it's been suggested that these diseases may have different genetic bases.⁶

Post et al. have suggested individuals with heightened susceptibility to bipolar disorder from genetic factors may experience several and increasing minor neurological insults, such as illicit drugs and chronic stress, which result in mania. If sufficient brain damage is undergone, mania will recur without the requirement of significant environmental or behavioral stressors. This proposed mechanism of bipolar disorder indicates that with every episode a sufferer undergoes, he or she increases his or her likelihood of having another in the future; it is therefore necessary that treatments of bipolar disorder are continuous and long-term.

Bipolar disorder remains a debilitating and dangerous reality for millions of people all over the world, interfering with an individual's ability to work, think, feel, or interact with those around him or her in significant and distressing ways. However, new researches into the causes of the disease, both on the genetic

⁶ O'Reilly, R. L.; Bogue, L.; Singh, S. M. : "Pharmacogenetic response to antidepressants in a multicase family with affective disorder." *Biol. Psychiat.* 36: 467-471, 1994.

and the neurological level, give hope to sufferers of the disease of advances in knowledge about their condition, and suggest that one day, medicine will finally be able both to cure and prevent this disorder.