

Genetics of Bipolar Disorder

Bipolar disorder (BP) is an illness characterized by periodic mania and often episodes of both depression and psychosis.¹ BP can be severely debilitating, and is accompanied by higher risk for suicide, poor quality of life, and lower productivity.¹ Approximately 0.5-1% of the population is affected by BP.²

BP is a complex disorder caused by both genetic and environmental factors. It is thought that heritability of BP is approximately 80%. Identification of the genes associated with BP has been difficult, likely because there are multiple genes that each contribute small effects to the phenotype.² Nevertheless, several genes that are promising candidates for BP have been identified through linkage and association studies. The findings implicate a number of different signaling pathways, such as the serotonergic, dopaminergic, neural development, cell growth/maintenance, and circadian pathways, in the control of BP.^{1,2} This suggests that BP is likely controlled by several different biological processes interacting with each other.^{1,2}

Both *SLC6A4* (the serotonin transporter) and *SLC6A3* (the dopamine transporter) have been identified as likely to control BP. Serotonin and dopamine are neurotransmitters that, among other functions, modulate mood. The transporters mediate the reuptake of serotonin and dopamine. Studies have identified polymorphisms in the transporters that are associated with symptoms of BP, suggesting that malfunction of the transporters contributes to the development of BP.² Additional evidence that alteration of the serotonin signaling pathway plays a role in BP is that polymorphisms in *TPH2*, an enzyme involved in the biosynthesis of serotonin, have been uncovered by association studies.²

The gene *BDNF* encodes a factor necessary for survival of striatal neurons in the brain. It has been found by a number of studies to be associated with BP. Although there is disagreement about the role of *BDNF* in BP,³ it continues to be studied as a possible player. Interestingly, the circadian rhythm pathway has been implicated in the susceptibility of BP.² Circadian rhythm genes regulate the timing of daily processes such as waking, body temperature, hormone levels, blood pressure and heart activity. Several new studies have uncovered associations between genes involved in the circadian pathway and BP.²

Genome-wide association studies continue to identify possible candidate genes for BP. Results are promising, but larger and more robust studies are needed.⁴ BP is a complex disorder, and it will likely take much work to piece together the many players and their roles in the susceptibility and development of the disorder.

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