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Using mathematical models of biological processes in genome-wide association studies of psychiatric disorders

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Using mathematical models of biological processes in genome-wide association studies of psychiatric disorders

Abstract

Genome-wide association studies have implicated a large number of genes in psychiatric disorders such as bipolar disorder and schizophrenia. These genes, however, are usually weakly-associated and involved in diverse biological processes, thereby obscuring mechanisms for how such disorders arise. To better elucidate mechanisms, disorders can be tested for association with a *set* of genes that represent a biological pathway. Even so, mechanisms can remain elusive if ultimately a specific biological function is important. We propose and analyze a statistical test to implicate biological functions in psychiatric disorders. Our approach relies on mathematical models of biological processes to predict how strongly genes contribute to a certain biological function. These predictions are used to assign *weights* to genes, which are then incorporated into a statistical test on genetic data. To demonstrate, we use this statistical test to explore the role of calcium signaling in bipolar disorder.