Multi-functional abnormality and bipolar disorder

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Background

Bipolar disorder (BD) is a chronic, severe psychiatric disorder with an estimated lifetime risk of about 1% (Ryan et al., 2006). Previously called manic depression, BD is one of the most challenging psychiatric disorders to manage. Patients are characterized by alternating episodes of mania and depression, accompanied by changes in activity associated with characteristic cognitive, physical, and behavioral symptoms (Anderson, Haddad, & Scott, 2012).

Proposed Approaches

1. We selected 12 sets of gene expression microarray data.
2. We used WABE (Weighing Arrays By Error, Chen et al.), t-test and MAQCm (Shi et al. 2006) to obtain differentially expressed genes between patients and healthy control, with which we then identify over-represented GO functions on bipolar affective disorder.
3. We ranked GO functions yielded by WABE by –log(p) value, then used the top 40% terms as key words to search the databases MEDLINE, PUBMED, and PsycINFO (1900-2013) for verification and annotation of our GO function results, and for the construction of BDFAM.

Motivations

Despite extensive research efforts, the underlying pathophysiology of BD remains unknown (Ryan et al., 2006). BD is a multi-system disorder, with symptoms likely caused by different diseases. To explore these causes, we obtained functional analysis of genomic profile of BD cohorts using multiple sets of gene expression microarray data. The purpose was to identify biological functions (as defined by Gene Ontology, or GO) associated with BD, to find relations among the functions, and to use these relations to construct a function association map for BD (BDFAM), thereby gaining insight to the systems property of BD.

Result 1: Three Protocols for Bipolar Collection

WABE yielded vastly more over-represented GO functions than t-test and MAQCm FDR=0.5 was used to call differentially expressed genes, when a smaller value FDR=0.05 was used, only yielded GO functions.

Result 2: Prominent GO functions found

A. Multi-organism processes (virus infection)

Several reports implicate: (AMP signaling plays a central role in the pathophysiology of mood disorders due to mediating responses of a number of pathways: e.g., dopamine.

B. Purine catabolism

Several reports suggest: (i) disease virus (Bow) causes several changes in brain functions resulting in mood, behavior, cognitive and neurocognitive disturbances including movement impairment.

Result 3- Used top 40% GO functions as key words to search databases

Verification by text-mining

Purine catabolism: Several reports implicate: Mitochondrial dysfunction merges into the pathophysiology of bipolar disorder, such as alterations of mitochondrial size, decrease in phosphocreatine and ATP etc.

Multi-organism processes (virus infection): Several reports suggest: (i) disease virus (Bow) causes several changes in brain functions resulting in mood, behavior, cognitive and neurocognitive disturbances including movement impairment.

Motivation: Mitochondrial dysfunction

Result 4 - Found relations among functions

A prominent interaction was “disruption”: if one function were disturbed, it might directly or indirectly affect other functions.

Summary: Our results suggest multi-functional abnormality as a cause of BD.