A deeper look onto Schizophrenia Mechanisms. Association with immunological related pathway

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Genetic liability factors of Schizophrenia have been identified but still a comprehensive picture is lacking. In the present work we focused on the genes previously associated with Schizophrenia and conducted a molecular pathway in a sample of schizophrenic patients and controls (~ 9000). A sample of bipolar patients and controls (~ 6000) served for replication. Data was retrieved from the public available NIMH database. A three steps analysis was undertaken: i) data of all the Genome Wide Association Analysis Studies (GWAS) on Schizophrenia published from 2007 to 2013 were collected; ii) a list of genes with a significant association with Schizophrenia was obtained and iii) the molecular pathways and sub-pathways associated with these genes were identified and tested for association with Schizophrenia. Finally, the most significant findings were replicated in the Bipolar sample. Some of the samples used for the analysis overlapped with the ones that provided the candidate genes. This work was then also used to test whether the molecular pathway analysis may give results consistent with the more classic GWAS approaches. A consistent find would pave the way to the use of this analysis in other independent datasets. As a result, a molecular pathway associated with immunologic activity was enriched in schizophrenic patients compared to controls (permutated (10^6) p = 0.037). Two genes (HLA-C and HLA-DRA) involved in this pathway were found to have more SNPs associated with both Schizophrenia and Bipolar Disorder than expected by chance. This result was consistent with the previous findings on GWAS studies, providing evidence that the molecular pathway analysis may be a rational approach to study Schizophrenia, with the advantage of providing complex pathways instead of single genes as a result.