Peripheral Blood Leukocyte RNA-Seq Identifies a Set of Genes Related to Abnormal Psychomotor Behavior Characteristics in Patients with Schizophrenia

Authors' Contribution:
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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Schizophrenia is a multigene disease with a complex etiology and different clinical manifestations. It is of great significance to understand the etiology and pathogenesis of schizophrenia patients from different clinical dimensions and to interpret the potential molecular changes of schizophrenia patients from different clinical dimensions.

Material/Methods: RNA-Seq was performed on peripheral blood leukocytes of 50 patients with schizophrenia and 50 healthy controls. Phenotypic information of patients with schizophrenia was collected during blood sampling. Differentially expressed genes (DEGs) were screened by the edgeR package of R software. To better analyze the correlation between DEG expression values, explore the potential association between differential genes and clinical dimensions of schizophrenia, and identify hub genes, we constructed a DEG co-expression network using weighted gene co-expression network analysis (WGCNA).

Results: We provide the transcription profiles of peripheral blood leukocytes in patients with schizophrenia and found a gene module (including 89 genes) closely related to the clinical dimension of abnormal psychomotor behavior in schizophrenia.

Conclusions: The findings enhance our understanding of the biological processes of schizophrenia, enabling us to identify specific clinical dimensions of genes for diagnosis and prognostic markers and possibly for targeted therapy.

MeSH Keywords: Gene Expression Profiling • Leukocytes • Schizophrenia

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Background

Schizophrenia is a common and difficult disease to treat clinically. Genetic factors play an important role in the pathogenesis of schizophrenia [1–3]. It is generally accepted that schizophrenia is a polygenic disease [4–7]. A single gene or SNP mutation site has little effect on schizophrenia [6]. Previous large-scale genome-wide association studies (GWAS) have found that multiple genetic *loci* are closely related to the occurrence of schizophrenia [8–10], however, identifying the risk chromosomes in schizophrenia is difficult. Great advancements have been made in genetic research on schizophrenia in recent years, with more than 100 genome-wide significant risk variations identified [10], but how reported risk variations affect the pathogenesis of schizophrenia remains elusive. Because schizophrenia is a mixed clinical syndrome, the clinical manifestations of schizophrenia vary. Some patients mainly have positive symptoms such as delusions and hallucinations [11,12]. Whereas, some patients mainly have negative symptoms such as apathy and decreased willpower [13,14]. Other patients have emotional symptoms such as mania or depression [15]. Schizophrenia is a heterogeneous aggregation of different clinical phenotypes. At present, clinical and basic research mostly focuses on schizophrenia itself. There are few studies on the relationship between different clinical manifestations and heredity. Defining the specific clinical dimensions of schizophrenia is a great challenge for psychiatrists.

In the past, the traditional clinical classification system classified schizophrenia as paranoid, catatonic, simple, undifferentiated, disorganized, and residual [16]. However, due to the heterogeneity of the disease, the stability of clinical diagnosis is poor, as is the standardization of treatment. Therefore, the 5th edition of the U.S. Diagnostic and Statistical Manual on Mental Illness (DSM-5; published in 2013) excludes these traditional subtypes of schizophrenia [17,18]. It is recommended that the psychiatric symptom severity rating scale be used to evaluate symptoms in different dimensions. In recent years, some scholars have divided the clinical manifestations of schizophrenia into the following 8 symptom groups (8-dimensional symptoms): abnormal psychomotor behavior, disorganized speech, hallucination, delusion, negative symptom, impaired cognition, depression, and mania [17,19,20]. This approach can deepen psychiatrists' further understanding of schizophrenia and guide clinical treatment and scientific research. Compared with the use of subtypes, the use of psychopathological dimensions in DSM-5 significantly improves the ability to describe the heterogeneity of the disease in a more effective and clinically useful way, and this approach can be targeted to different dimensions of symptoms for research and treatment [19–22].

To further study the relationship between different dimensions of schizophrenia and heredity, we collected clinical information from schizophrenia patients and used the dimension method in DSM-5 (Clinician-Rated Dimensions of Psychosis Symptom Severity scale) to assess the severity of the core symptoms of schizophrenia [19,20]. If the score of the core symptoms in a dimension was 2 or greater than 2, we considered the symptoms in this dimension to be positive. If the score of the core symptoms in a dimension was less than 2, we considered the symptoms in this dimension to be negative [17,19]. The total RNA of peripheral blood leukocytes from study participants was collected at the same time as the dimension score assessment. After removing ribosomal RNA (rRNA), the DNA library was constructed. Illumina HiSeqTM 4000 sequencing technology was used to obtain information on the transcription groups and to explore the differences in genes between 2 groups: schizophrenia patients and healthy controls who were roughly matched for sex and age. Weighted gene co-expression network analysis (WGCNA) was used to analyze the relationship between differential genes and 8 clinical dimensions. Interestingly, we found that Turquoise module was positively correlated with abnormal psychomotor behavior, and the difference was statistically significant. We randomly selected 5 hub genes (*CXCL8, EGR1, EGR3, IL1B,* and *PTGS2*) for quantitative analysis. Quantitative real-time polymerase chain reaction (qRT-PCR) validation showed that the results were consistent with those of messenger RNA (mRNA) sequencing. In our study, the Turquoise module (89 genes) was identified as new risk genes for the abnormal psychomotor behavior dimension of schizophrenia, and we speculate that risk variation might affect the expression of these genes. This leads to the susceptibility of patients with schizophrenia to the abnormal psychomotor behavior dimension.

Material and Methods

Study patients

A total of 50 patients with schizophrenia were enrolled from the Honghe Second People's Hospital and Yuxi Second People's Hospital from May 2018 to July 2018. During the same period, 50 healthy volunteers with similar sex and age were recruited into the normal control group at the Sixth Affiliated Hospital of Kunming Medical University. After the patients with schizophrenia and healthy controls provided informed consent, we used anticoagulant extraction to obtain 5 mL of peripheral blood.

Inclusion criteria for the patient case group

Inclusion criteria for the patient case group were as follows: 1) meet the criteria for diagnosis of schizophrenia in DSM-5; 2) first onset schizophrenia or no antipsychotic drugs for 5

weeks before enrollment; 3) Han Chinese aged 18 to 60 years; 4) no significant RNA degradation in the sample; and 5) signed informed consent and voluntary participation in this study.

Exclusion criteria for the patient case group

Exclusion criteria for the patient case group were as follows: 1) combination of mental disorders caused by other mental illnesses such as depression or physical and physical diseases; 2) serious neurological diseases or severe physical diseases such as the combination of liver and kidney insufficiency; 3) a medical history of alcohol dependence, substance abuse and addiction; 4) a history of blood transfusion within 1 month before admission; 5) treatment with electroconvulsive therapy (ECT) within 3 months; and 6) severe audio-visual disorders and intellectual development disorders.

Inclusion criteria in the healthy control group

Inclusion criteria for the health control group were as follows: 1) a normal physical examination of adults without abnormalities, without any family history of mental illness; 2) no history of severe traumatic brain injury, no neurological diseases, and no major physical diseases and trauma history; and 3) of Chinese Han nationality roughly matched with the sex and age of the case group.

Ethical approval and informed consent of patients

All experimental schemes involving human participants in this study were approved by the Ethics Committee of the Sixth Affiliated Hospital of Kunming Medical University. All participants in the study provided written informed consent, and all participants agreed to use their clinical and RNA-Seq data for research and publication. The research methods adopted were based on the Helsinki Declaration and the guidelines of the Ethics Committee of the Sixth Affiliated Hospital of Kunming Medical University. Patients were told that refusing to participate in the study would not affect future treatment.

Peripheral blood leukocyte (PBL) collection and total RNA extraction

Collection of fresh whole blood samples

At approximately 7: 00 a.m., 5 mL of whole blood was extracted by venipuncture from the study participants. An EDTA anticoagulant tube was used. The samples used to extract leukocyte RNA were centrifuged within 60 minutes and transferred to a 1.5 mL EP tube. The leukocytes were mixed with 1 mL TRIzol and then transferred into a 1.5 mL freezer tube (which was tightly sealed with sealing film and stored in liquid nitrogen or –80°C freezer.

Total RNA extraction

TRIzol reagent (Invitrogen, Carlsbad, CA, USA) was used to extract leukocytes from peripheral blood. A Nanodrop ND200 (Thermo Scientific Inc., Waltham, MA, USA) was used to determine the concentration and purity of RNA. According to OD260, the concentration of the RNA sample was calculated as follows: RNA (mg/mL) = 40×OD260×dilution multiple/1000. The value of OD260/OD280 of pure RNA is generally 1.8–2.0, so the purity of RNA can be estimated according to the value of OD260/OD280. If the ratio is low, there are residual proteins. It is important to note that the value of RNA OD260/OD280 extracted by this method was between 1.8 and 2.0 (hands are the main source of RNase).

Library construction sequencing

After extracting the total RNA, the rRNA was removed using the Ribo-ZeroTM Magnetic Kit to enrich the mRNA. The enriched mRNA fragments were then converted into short fragments with fragmentation buffer, and the cDNA was reversed transcribed with a random primer. Second chain cDNA was synthesized with DNA polymerases I, RNase H, DNTP, and buffers. The samples were then amplified using QIAquick-PCR to purify the cDNA fragments, repair the ends, add polyadenine (a), and connect the Illumina sequencing adaptor. The product was sequenced with the Illumina HeSeqTM 4000, and underwent agarose gel electrophoresis and PCR amplification at Gidio Biotechnology (Guangzhou, China).

Analysis of differential expression transcription products (DEGS) of coding RNA

To identify differentially expressed transcripts between the schizophrenia patients and the healthy controls, the edgeR package (*http://www.r-project.org/*) was used [23] and Benjamini-Hochberg (B-H) correction for multiple comparisons. We categorized the transcripts with multiple fold changes (>2) and false discovery rate (FDR) <0.05 as indicting significant differentially expressed genes (DEGs). Then, enrichment analysis of Gene Ontology (GO) function and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was carried out for differentially expressed coding RNA.

Comparison of our RNA sequencing of differential genes with genes identified by GWAS identification and genes identified by gene set enrichment (GSE) data set

We downloaded the GWAS identification gene on SZDB data [24] (*http://www.szdb.org/SZDB/gwas.php*) and several data sets from the GEO public data set (GEO, *http://www.ncbi. nlm.nih.gov/geo*), including GSE62191 (comprising 29 patients with schizophrenia and 30 healthy controls) [25,26], GSE17612

Table 1. Primer sequences.

Genes	Forward	Reverse
EGR1	GGTCAGTGGCCTAGTGAGC	GTGCCGCTGAGTAAATGGGA
EGR3	GACATCGGTCTGACCAACGAG	GGCGAACTTTCCCAAGTAGGT
IL1B	ATGATGGCTTATTACAGTGGCAA	GTCGGAGATTCGTAGCTGGA
CXCL8	AAGACATACTCCAAACCTTTCCACC	CTTCAAAAACTTCTCCACAACCCTC
PTGS2	CTGGCGCTCAGCCATACAG	CGCACTTATACTGGTCAAATCCC
ACTB	CATGTACGTTGCTATCCAGGC	CTCCTTAATGTCACGCACGAT

(including 28 patients with schizophrenia and 23 cases of healthy controls) [27], and GSE12649 (including 35 patients with schizophrenia and 34 cases of healthy control) [28]. First, GEO2R was used to identify the differential genes between the schizophrenia group and the healthy control group in the GSE dataset. With *P* less than 0.05 indicating statistical significance (GSE dataset differential gene results are detailed in Supplementary Document 1), a Venn diagram was drawn using the Omicshare tool, a free online data analysis platform (*www.omicshare.com/tools*).

WGCNA analysis

The WGCNA algorithm is a common algorithm for building gene co-expression networks. The WGCNA algorithm first assumes that the gene network obeys the scale less distribution, defines the adjoining function of the gene co-expression correlation matrix and gene network formation, calculates the difference coefficient of different nodes, and constructs a hierarchical cluster tree accordingly. Different branches of the cluster tree represent different genetic modules. The degree of gene co-expression is high, while the degree of gene co-expression is low in different modules. Finally, the relationship between the module and the specific phenotype was explored, and the target gene and gene network of the disease-specific phenotype were finally obtained. We extracted 559 upregulated and downregulated DEGs from edgeR analysis and performed WGCNA with the expressed sequencing data [29]. The R-package "WGCNA" was used to search for related modules and hub genes of clinical traits.

Analysis of trait-related characteristics module

The main goal of network co-expression analysis is to identify the modules and genes most relevant to biological significance or clinically relevant. Hence, the modules most relevant to the traits for schizophrenia were identified by analyzing the correlation between the modules and specific phenotypes or traits. By calculating the correlation between each module's characteristic values and traits, we identified the modules and genes most relevant to the traits so that the corresponding modules could be selected for further study. In general, if a module has a significantly higher correlation with the selected trait than the other modules, it indicates that the module may have the strongest correlation with the trait. The grouping relationship is considered a trait used to determine the relationship between modules and groupings. Then, the gene function of a clinical dimension-related (and statistically significant) module was analyzed, and the GO and KEGG pathways were enriched to analyze the biological function of the module.

Protein–protein interaction (PPI) network analysis

Protein–protein interaction (PPI) was used to find the biologically or clinically meaningful modules and analyze the gene expression profiles of the study patients. Each gene in the module was calculated; the highly connected genes are often hub genes, which may have important functions. The network was visualized using String database (*http://www.string-db.org/*).

qPCR verification

Illumina offers a wide range of powerful library preparation kits that provide fast and easy library preparation workflow, and the Illumina HiSeqTM 4000 sequencing results are highly technically repeatable. However, to further verify the accuracy of our peripheral white blood cell sample sequencing results, we used qRT-PCR to validate 5 hub genes (*CXCL8*, *EGR1*, *EGR3*, *IL1B*, and *PTGS2*) in the Turquoise module to evaluate whether the results were consistent with mRNA sequencing results and to verify the accuracy of the Illumina HiSeqTM 4000 sequencing results. Extracted RNA was synthesized with complementary DNA (cDNA) using a reverse transcription kit (Takara). Real-time PCR was carried out with TB Green series kit (Takara) and monitored with the Bio-RAD (CFX96 real-time) system. β-actin for mRNA was applied to normalize the result. All reactions were repeated 3 times and relative gene expressions were evaluated by the $2^{-\Delta\Delta Ct}$ method. Primer sequences are shown in Table 1.

Statistical methods

All transcript sequencing data were analyzed by R software. GEO data sets were analyzed by GEO2R tools, and qRT-PCR validation data were tested by 2 independent samples *t*-test. The test level a=0.05, *P*<0.05 was considered statistically significant.

Results

Analysis of the difference in the expression of mRNA between the 2 groups

We used edgeR software to analyze the difference in FPKM (fragments per kilobase of transcript per million) values between the healthy control group and schizophrenia patients. FDR and log2FC were used to screen differential transcripts. The screening conditions were FDR <0.05 and |log2FC| >1. A total of 559 differentially expressed transcripts were screened, including 206 downregulated transcripts and 353 upregulated transcripts (see Supplementary Table 1 for details). Also, we compared with GWAS and other brain GSE datasets and used

a Venn map (Figure 1A–1E). The comparisons between GWAS identifying genes and GSE dataset identifying genes in brain regions can be found in the Supplementary Document 1; a Venn chart compared GWAS and GSE data.

Differential mRNA GO/pathway enrichment analysis

After obtaining differentially expressed transcripts, GO functional analysis and KEGG pathway analysis were performed on the differentially expressed transcripts. Taking FDR <0.05 as the threshold, we calculated the *P* values. Meeting this condition was defined as a significant enrichment GO item in DEGs. This analysis can identify the main biological functions performed by different genes. GO analysis indicated that DEGs were mainly concentrated in response to stress, immune system process, and immune response, as shown in Figure 1F. The KEGG pathway analysis showed that DEGs are mainly involved in mineral absorption, IL-17 signaling pathways, etc. The KEGG enrichment analysis chart is shown in Figure 1G.
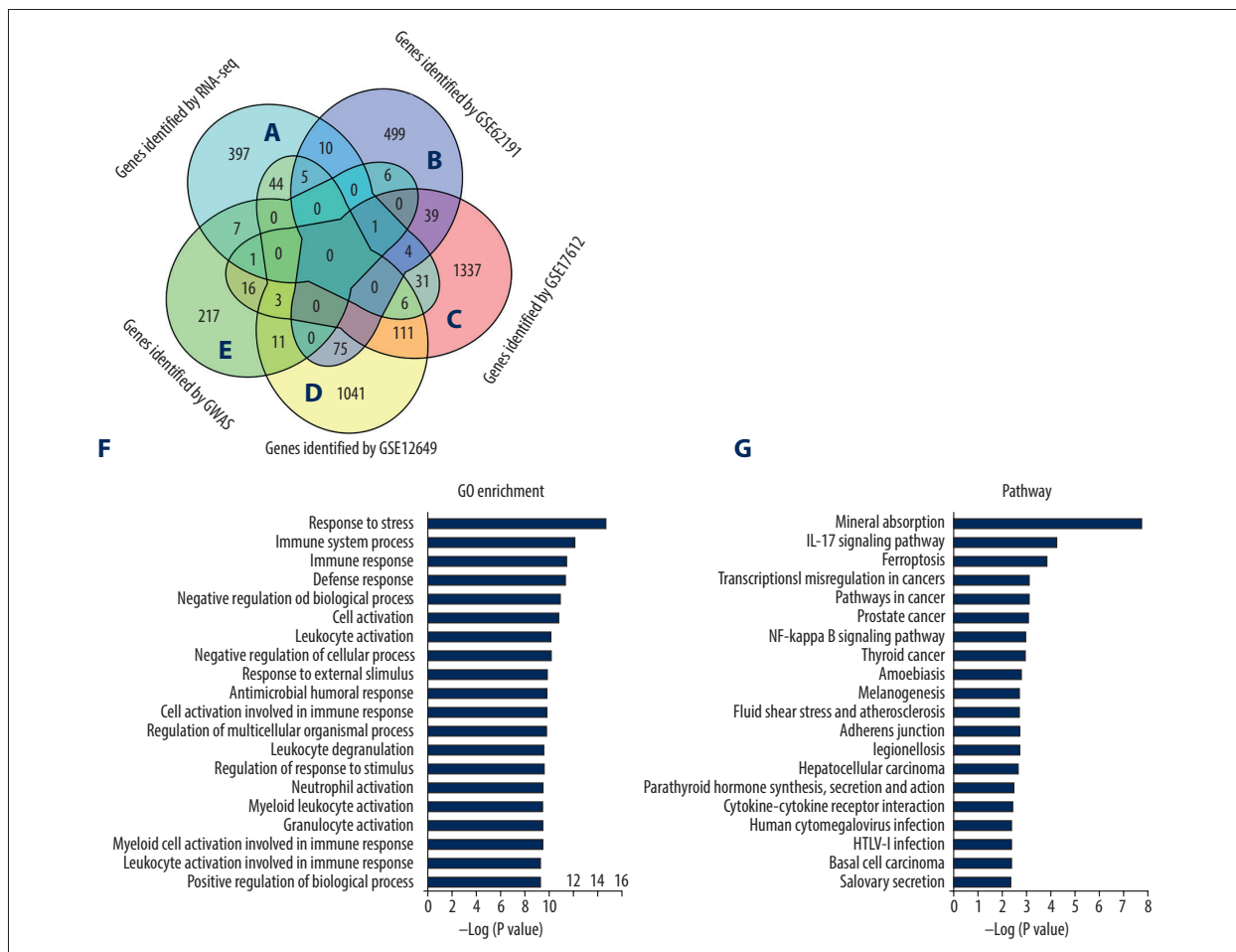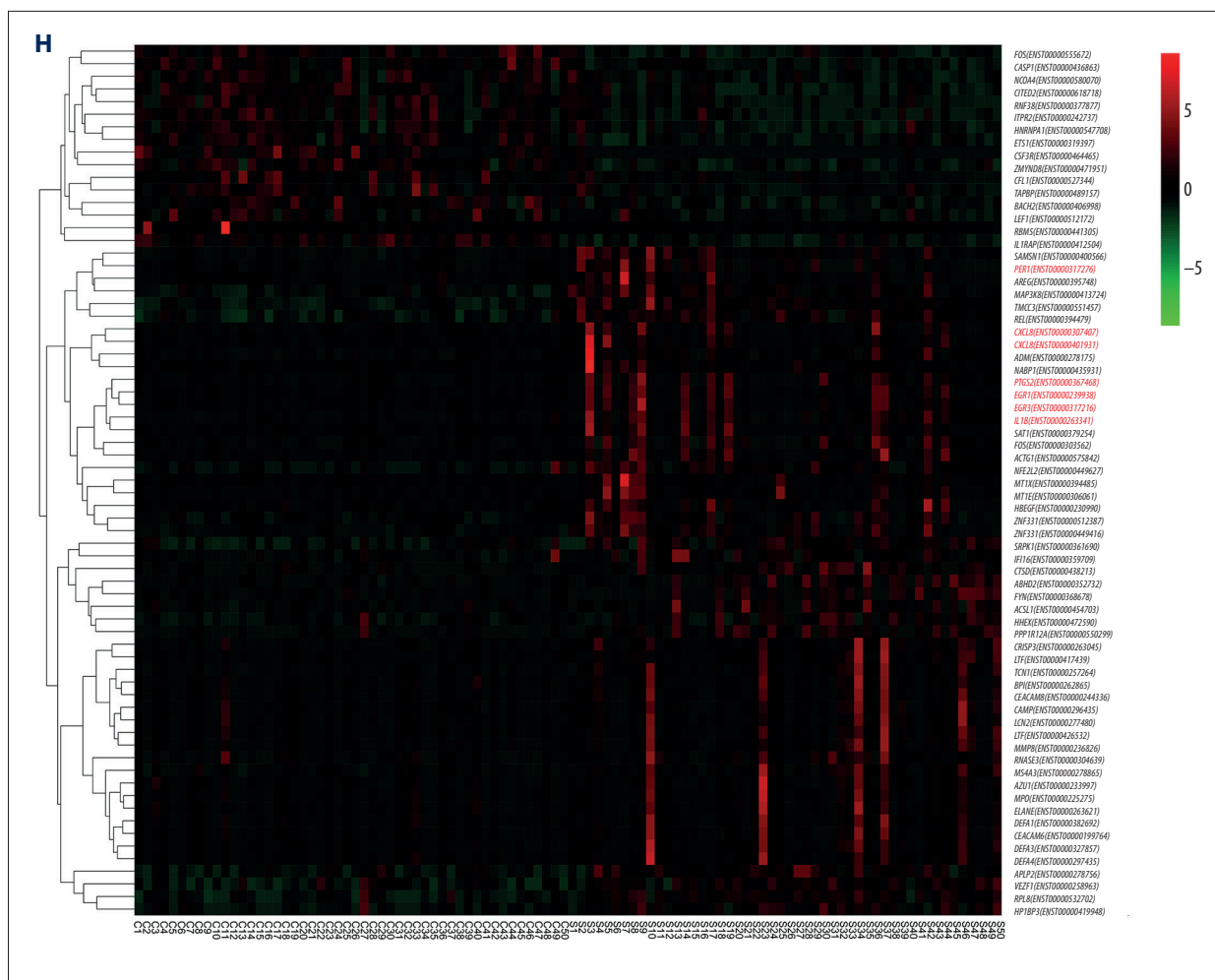
Figure 1. (**A–E**) Comparisons between genome-wide association studies (GWAS) and gene set enrichment (GSE) dataset. Identifying genes in the brain regions can be found in Supplementary Document 1 Venn chart that compares GWAS and GSE data. (**F**) Gene Ontology (GO) item in differentially expressed genes (DEGs). (**G**) The Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis chart. (**H**) Expression patterns of differentially expressed transcripts (69 transcripts) with an average value of FPKM (fragments per kilobase of transcript per million) greater than 1 in the healthy control group and schizophrenia group and constructed a heat map.

Cluster analysis of expression patterns

Based on the expression of transcripts, the relationship between transcripts was hierarchically clustered, and the clustering results were presented using a heat map. We analyzed the expression patterns of differentially expressed transcripts (69 transcripts) with an average value of FPKM greater than 1 in the healthy control group and schizophrenia group, and we constructed a heat map (Figure 1H). The rows were normalized (z-score), and hierarchical clustering analysis was carried out for different transcripts. Each column in the graph represents one sample: C1–C50 are the 50 samples of the healthy control group, and S1–S50 are the 50 samples of the schizophrenia group. Each row represents one transcript, and the expression of transcripts in different samples was expressed in

different colors. The redder the color, the higher the expression level, and the greener the color, the lower the expression level.

WGCNA module division

The adjacency matrix was transformed into a topological overlap matrix. According to the TOM-based difference measure, genes are divided into different gene modules. According to the principle of a scale-free network, the power value was determined. The power value selected in this analysis was 5. The parameters (similarity) of the merging module were 0.75, and the number of genes needed to be included in each module was at least 30. The hierarchical clustering tree of modules is as follows: 1) Dynamic Tree Cut is a module divided according to clustering results, 2) Dynamics is a combined module division
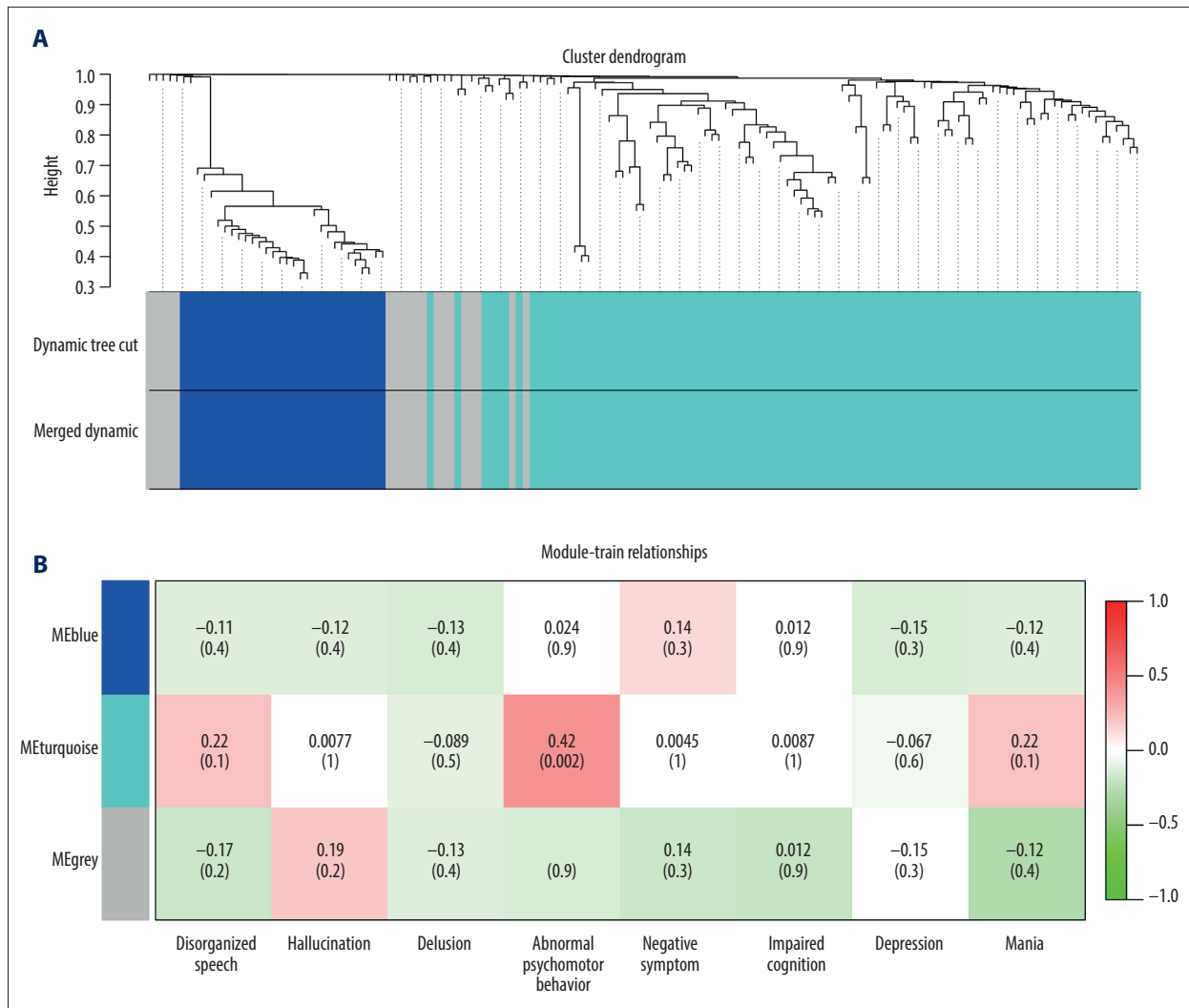
Figure 2. (**A**) The hierarchical clustering tree of modules. (**B**) The results of the trait-module correlation are shown in the Module-Trait Relationships chart.

of modules that express similar patterns based on module similarity, followed by analysis according to the merged module, and 3) for Tree Diagrams, vertical distance represents the distance between 2 nodes (between genes), and the horizontal distance is meaningless. See Figure 2.

Character module analysis

The main goal of the network co-expression analysis was to identify the most relevant modules and genes of biological of clinical significance. Therefore, the most relevant modules can be found by analyzing the correlation between modules and specific phenotypes or traits. By calculating the correlation between each module's characteristic values and traits, we can identify the modules and genes most relevant to the traits, so that the corresponding modules can be selected for further study. In general, if one module has a significantly higher

correlation with the trait than the other modules, this indicates the module may have the strongest correlation with the trait. The 8-dimensional characteristics of schizophrenia samples are detailed in Supplementary Table 2: Schizophrenia Sample Trait. The grouping relationship was used to find the relationship between the module and the grouping. The results of the trait-module correlation are shown in the Module-Trait Relationships chart (Figure 2B) which contains the correlation coefficients and *P* values of each trait and module characteristic values.

Each column of the Profile-Related Characteristics Module (Figure 2B) represents a personality, and each row represents a genetic module. The number in each box represents the correlation between the module and the characteristic. The closer the number is to 1, the stronger the positive correlation between the module and the characteristic. The closer the module to −1, the stronger the module's negative correlation with the trait.
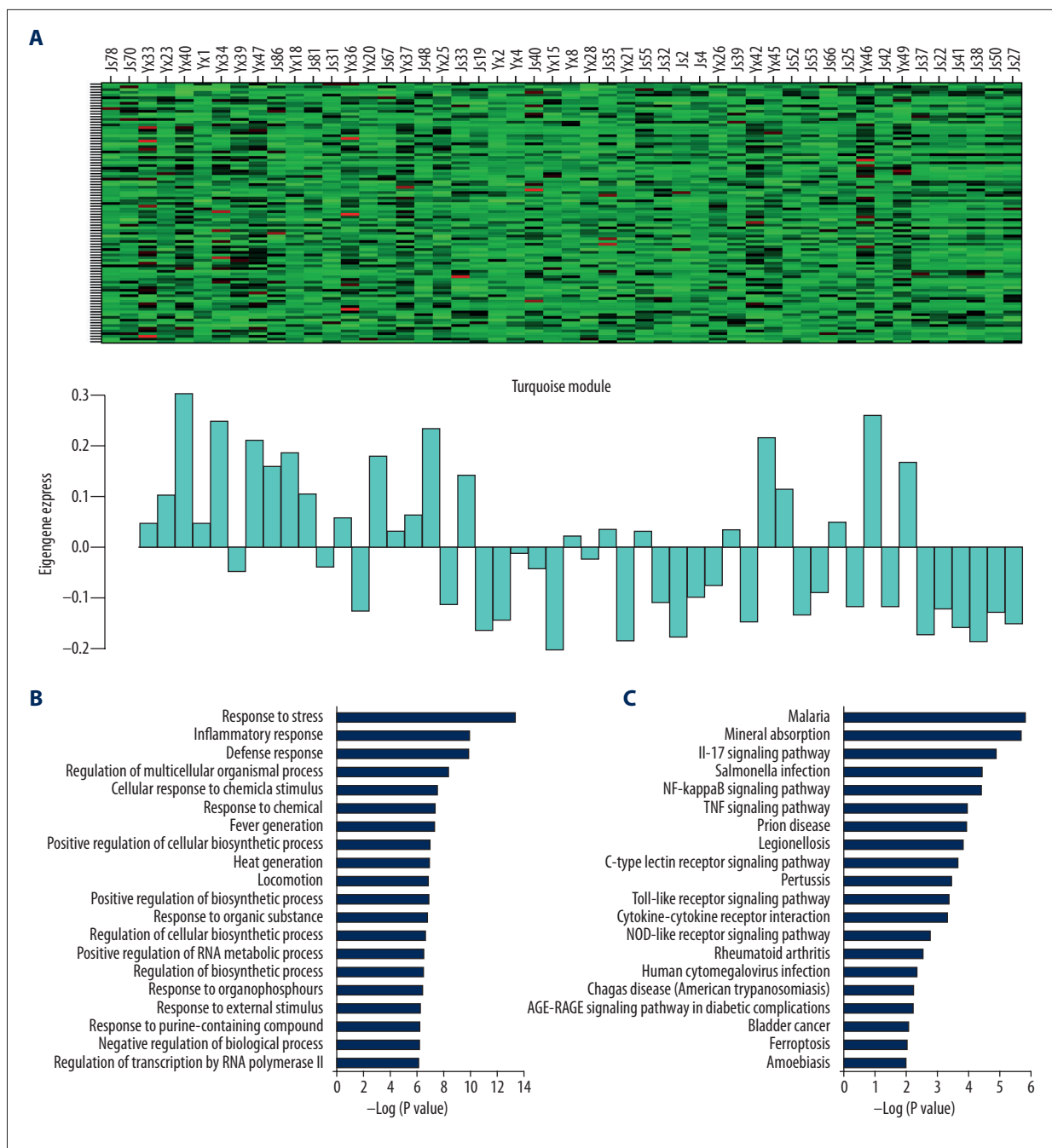
Figure 3. (**A**) Expression patterns of the genes contained in the Turquoise module. (**B**) The Gene Ontology (GO) enrichment analysis of the genes contained in the Turquoise module. (**C**) Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of the genes contained in the Turquoise module.

The numbers in parentheses represent the significance of the *P* value, and the smaller the number, the greater the significance. The *P* value was calculated using the Student's *t*-test, the smaller the *P* value, the more significant the correlation between the representative form and the module. The results suggest that the Turquoise module is positively correlated with abnormal psychomotor behavior (*P*=0.002).

Turquoise module gene expression pattern and functional enrichment

We show the expression patterns of the genes contained in the Turquoise module using thermal maps and changes in the module's eigenvalues in different samples (equivalent to the module expression pattern) by histogram, as shown in Figure 3A.

Figure 4. Turquoise modules to string, a protein–protein interaction (PPI) network was generated.

The calorimetric expression of genes in different samples is shown. Red indicates upregulated genes, and green indicates downregulated genes. The expression pattern of module eigenvalues in different samples is shown. GO analysis reveals that the Turquoise module genes are mainly concentrated in biological processes, such as response, locomotion, immune system process, cell motility, and localization of cells. The GO enrichment analysis is shown in Figure 3B. The KEGG pathway analysis (Figure 3C) shows that the Turquoise module genes are mainly involved in malaria, mineral absorption, the IL-17 signaling pathway, Salmonella infection, the NF-κB signaling pathway, and the tumor necrosis factor (TNF) signaling pathway.

PPI network construction and hub gene analysis

After mapping the genetic symbols of all the Turquoise modules to String, a PPI network (Figure 4) was generated. PPI statistical analysis indicates 89 nodes with 141 edges; the average node degree was 3.17, the expected number was 57, and PPI p-enrichment was 1.0e-16. At the same time, we selected the hub gene using the CytoHubba plug-in in Cytoscape to determine the top 20 hub genes with high connectivity in turn: *CXCL8, FOS, PTGS2, IL1B, ATF3, EGR1, CXCL2, REL, NFE2L2, SNAI1, PLAU, HBEGF, AREG, EGR2, ETS1, PTGER3, LEF1, ADM, SERPINB2,* and *EGR3.*

Figure 5. (**A–E**) Quantitative Real-Time polymerase chain rection results of 5 hub genes in the Turquoise module.

Gene validation

To further verify the accuracy of the sequencing results of our peripheral blood leukocyte samples, we randomly selected 5 hub genes (*CXCL8, EGR1, EGR3, IL1B,* and *PTGS2*) in used the Turquoise module for qRT-PCR verification. Two independent sample *t*-tests showed that the expression of *CXCL8, EGR1, EGR3, IL1B,* and *PTGS2* in the schizophrenia group was higher than that of the healthy control group (*P*<0.05). The qRT-PCR results were consistent with those of mRNA sequencing (Figure 5).

Discussion

Information regarding mRNA expression in the brain of patients after death is very important to elucidate the molecular genetic mechanism of schizophrenia and other neuropsychiatric diseases. However, brain tissue specimens from living patients are difficult to obtain. Recent studies have found that the immune system plays a vital role in the repair, maintenance, and brain reserves of the central nervous system [30,31], that immune cells help maintain neurogenesis and spatial learning in adulthood [32], and that age-related spatial memory loss can be partially recovered through immune activation [33]. The interaction between neurons, glial cells, and the immune system contributes to the healthy functioning of the brain [34]. The occurrence of schizophrenia is closely related to immunity [35]. Peripheral blood macrophage/monocyte inflammation patterns may indicate the activation of small glial cells, which, in the brain, are macrophages, and are considered the main immune cells [36]. Neuroimmune interactions allow the nerves and immune systems to regulate each other: immune cells play an important role as peripheral neurotransmitters, peripheral T cells exhibit similar characteristics as dopamine-activated cells, and the brain can regulate immune cells [37]. The cells that compose the peripheral immune system are mainly white blood cells, which are easy to collect in a clinical setting and can be used as an alternative to brain tissue for biomarker screening studies.

The results of this study can help us understand the relationship between different dimensions of schizophrenia and genetics. In the past, genetic studies of schizophrenia have paid little attention to its heterogeneity (and little attention to symptom dimensions). In this study, we describe a large transcription dataset of blood cells in a patient with schizophrenia (detailing their symptom dimensions) as well as gender and age-matching control samples of white blood cells.

First, we analyzed the differential expression patterns of transcripts between the schizophrenia group and the healthy

control group. A total of 559 differential transcripts (506 genes) were found. Functional enrichment analysis of differential genes indicated that 139 transcripts were involved in response to stress biological processes (GO: 0006950), and 114 transcripts were involved in immune system processes (GO: 0002376). Enrichment analysis indicated that 93 transcripts were involved in immune response processes (GO: 0006955). DEGs were mainly involved in the immune response, IL-17 signaling pathway, and NF-κB signaling pathway. Dimitrov et al. showed that the IL-17 signaling pathway may play an important role in schizophrenia [38]. Numerous studies have shown that the NF-κB signaling pathway plays an important role in nerve protrusion growth, activity-dependent plasticity, and cognitive function, and that abnormal changes in the NF-κB signaling pathways in patients with schizophrenia can occur [39,40].

A Venn diagram was used to analyze where the DEGs identified by RNA-Seq and the genes identified by GWAS overlapped. A total of 9 overlapping genes (*LRP1, ABCB9, NISCH, EGR1, FES, DGKZ, FYN, CTND1,* and *ALDOA*) were found. GSE62191 had 20 overlapping genes, GSE12649 had 55 overlapping genes, and GSE17612 had 43 overlapping genes. Our study found that *FOS, IL1B, CXCL8, CASP1, CFL1, CAMP, ITPR2, ACTG1* and other inflammation and immunity related genes were differently expressed between the schizophrenia patient group and the healthy control group, These findings were consistent with the neuroinflammatory hypothesis of schizophrenia. Previous studies have shown that the loss of mTOR inhibitor *TSC1* or *PTEN* can increase the growth of somatic cells and dendrites, and that altered TSC/mTOR or PTEN/mTOR signal can play an important role in the development of autism spectrum disorders [41–44]. In our study, we found that the ASD related genes *PTEN, mTOR, TSC1,* and *FMR1* expression in peripheral blood of patients with schizophrenia had no significant change when compared with healthy controls. This may indicate that these 2 common psychiatric diseases have different pathogenesis. According to the differential gene thermogram, the expression of *CASP1* and other genes in schizophrenia patients decreased significantly. *CASP1* is a risk gene for depression [45,46]. At present, there are no studies on the relationship between *CASP1* and schizophrenia. Some studies found that the depression-like symptoms of *CAPS1* knockout rats were alleviated, while pleasure-like behaviors occurred, and the speed of exercise was increased in rats [45]. The decreased expression of *CASP1* in patients with schizophrenia may be related to the positive symptoms of patients with schizophrenia, and the specific role of *CASP1* in schizophrenia is unclear. We need to conduct more research on *CASP1* in the future.

To find the key module most relevant to the clinical dimension of schizophrenia, we carried out WGCNA on DEGs using edgeR analysis. Clinical sample information was collected from patients, such as abnormal psychomotor behavior, disorganized speech, hallucination, delusion, negative symptom, and 8 other dimensions. Through WGCNA of differential transcripts, we determined 3 modules (nonclustering degree of gray display). From the thermogram of the module-feature correlation, we found that the Turquoise module was the module that was most correlated with the clinical features of abnormal psychomotor behavior, and the correlation coefficient was 0.42, *P*=0.002. The Turquoise module contains 96 transcripts (89 genes). We used the CytoHubba plug-in in Cytoscape to select hub genes and identify the top 20 hub genes with high connectivity: *CXCL8, FOS, PTGS2, IL1B, ATF3, EGR1, CXCL2, REL, NFE2L2, SNAI1, PLAU, HBEGF, AREG, EGR2, ETS1, PTGER3, LEF1, ADM, SERPINB2,* and *EGR3.* To reveal the potential biological functions of genes in the Turquoise module, we performed GO and KEGG analysis. This analysis shows that the genes in the Turquoise module are mainly involved in the response to stress, inflammatory response, locomotion, immune system processes and other biological processes. *ADORA3, IL1B, ADM, FOS, CXCL8, PER1, ETS1, LRP1, IFI16, PTGS2, PTGER3, REL, IL1RAP, HRH4,* and *CXCL2* were involved in inflammatory response (GO: 0006954), This indicated that inflammation related genes play an important role in the abnormal psychomotor behavior characteristics in patients with schizophrenia, These results provide a new clue for further study of the mechanism of abnormal psychomotor behavior in schizophrenia. The Turquoise module contains 5 genes (*CXCL8, FOS, PTGS2, IL1B,* and *CXCL2*) enriched in the IL-17 signaling pathway, 5 genes (*PLAU, IL1B, CXCL2, CXCL8,* and *PTGS2*) enriched in the NF-κB signaling pathway, 3 genes (*IL1B, FYN,* and *EGR1*) enriched in prion diseases, 6 genes (*FOS, MAP3K8, IL1B, CXCL2, BCL3,* and *PTGS2*) enriched in the TNF signaling pathway, and 4 genes (*FOS, MAP3K8, IL1B,* and *CXCL8*) enriched in the Toll-like receptor signaling pathway. Previous studies have found that the TNF signaling pathway and Toll-like receptor signaling pathway are closely related to the onset of schizophrenia [47–49].

WGCNA identified 89 risk genes for schizophrenia (Supplementary Table 3), and their expression changes were positively correlated with abnormal psychomotor behavior in schizophrenia. The Turquoise module contains 3 genes of the *EGR* family (*EGR1, EGR2,* and *EGR3*). Hub gene *EGR1* plays an important role in the occurrence of schizophrenia. Kurian et al. [50] suggested that *EGR1* gene expression is increased in the blood of patients with schizophrenia who have a high illusion state. Other studies have shown that *EGR1* is downregulated in the prefrontal cortex of postmortem brain samples from patients with schizophrenia [51,52]. Ramaker et al. [53] performed transcriptome analysis of 24 patients with schizophrenia and 24 bipolar disorder patients and 24 control brain tissues. The results showed that the expression of *EGR1* in the anterior cingulate cortex of patients with schizophrenia was significantly lower than that of the control group. Studies have found that *EGR3* is considered a potential susceptibility gene for

schizophrenia [54–56]. *CXCL8* is a risk gene for depression [57], but recent studies have shown that chemokine *CXCL8* is involved in the neurobiological process associated with schizophrenia. The increase in maternal *CXCL8* levels is also related to the increased risk of mental illness in offspring [58–60]. The *PTGS2* gene, also known as the *COX2* gene, is closely related to schizophrenia. The *PTGS2*-specific inhibitor has a curative effect on schizophrenia [61,62].

Our data showed that there was a significant difference in gene expression between the schizophrenia group and the healthy control group. Further analysis of the gene and clinical phenotype by WGCNA suggested that the Turquoise module in patients with schizophrenia was significantly related to abnormal psychomotor behavior, among which key genes were involved. *IL1B* participates in 5 pathways, thus, we speculate that *IL1B* in core genes may lead to abnormal psychomotor behavior in schizophrenia through the IL-17 signaling pathway, NF-κB signaling pathway, TNF signaling pathway, and Toll-like receptor signaling pathway. In addition, these data provide useful resources for future research and help to test preliminary hypotheses or verify important findings.

Conclusions

In the present study, compared with the healthy control group, 206 downregulated transcripts and 353 upregulated transcripts were found in the schizophrenia group samples. Functional analysis of GO showed that DEGs were mainly enriched in

response to stress, immune system process, and immune response. The KEGG pathway analysis showed that DEGs mainly participated in the TNF signaling pathway and the IL-17 signaling pathway. WGCNA divided DEGs into 3 co-expression modules, which indicated that the Turquoise module was positively correlated with abnormal psychomotor behavior (*P*=0.002). We randomly selected 5 hub genes (*CXCL8*, *EGR1*, *EGR3*, *IL1B*, and *PTGS2*) of the Turquoise module for qRT-PCR verification. The results of qRT-PCR were consistent with those of mRNA sequencing. We provided the transcription profiles of peripheral blood leukocytes in patients with schizophrenia and found a gene module (including 89 genes) closely related to the clinical dimension of abnormal psychomotor behavior in schizophrenia. We also speculate that *IL1B*, a hub gene, may play an important role in the abnormal psychomotor behavior of schizophrenia through multiple pathways. These findings enhance our understanding of the biological processes of schizophrenia, enabling us to identify specific clinical dimensions of genes for diagnosis and prognostic markers and possibly for targeted therapy

Acknowledgements

Conflict of interest

None.

Supplementary Data

Supplementary Document 1.

1. Genes identified by GSE62191

KRT6A, TNFSF10, GBP4, SLC14A1, SCGB1D2, DUSP1, FAM86B3P, ETV5, ARC, KIF19, DUSP6, PLIN1, TTC7A, KDF1, USP45, ZMYM5, ELK3, SPAG5-AS1, PLPP5, SCGB1D1, FKBP5, CBX3P2, HSPA8, CCT6P1, C1orf74, EGR2, HES4, DYRK1A, PGBD1, PROCR, DYNLL2, RHCE, EIF3F, SERPIND1, CRTAM, EPM2A, CLEC18A, CASP14, NHLRC2, LIF, VEGFC, DUSP5P1, ATP13A4, DUS4L, GLI2, TEX2, SPRR2C, ZNF615, LOC158435, EGR1, DCAKD, CD52, EGR4, PER2, TTC13, HLA-DRB3, TTC33, GPR149, MRVI1, HRAS, SAMHD1, MDC1, GPR20, ALDH1L1, TRPC3, GNAZ, USF2, CCND1, TRIM24, PDZD2, MOCOS, PTPN7, PAPSS1, SMCHD1, BBS2, TSACC, PRR15, CD69, CCL4, EGFR, PIGA, ATP1B2, F7, SDC4, TRPV2, TECPR2, MCM6, LOC100129397, MFGE8, ZNF442, SLC25A21-AS1, LINC00469, GALNT4, CD1B, LOC101927598, OR7G3, C2CD4B, SLC15A2, WNT7A, CALML4, RRN3, SOD3, AQP1, PGM5, IRX6, CPZ, ITPKB, DGKE, WHSC1L1, HIF3A, DNAJB6, CMYA5, SERBP1, FAM161A, TMPRSS5, NR3C1, PLAU, MLXIPL, SNX2,

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2. Genes identified by GSE17612

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CLINICAL RESEARCH

3. Genes identified by GSE12649

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4. Genes identified by GWAS

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Supplementary Table 1. Differentially expressed mRNAs in peripheral blood Leukocyte from Schizophrenia patients versus healthy controls by RNA-seq.

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000010404	0.0006	0.067	6.803055	0.000242	MGST1
ENST00000064780	0.343	0.9742	1.506009	5.61E-05	RELT
ENST00000164227	0.001	0.081	6.33985	3.93E-05	BCL3
ENST00000199764	1.007	2.7254	1.436404	0.00132	CEACAM6
ENST00000204726	0.001	0.0072	2.847997	0.000598	GOLGA3
ENST00000216127	0.0028	0.027	3.269461	0.000102	RASD2
ENST00000218432	0.1038	0.2788	1.425424	0.000598	PIN4
ENST00000221327	0.0432	0.3458	3.000835	1.81E-05	ZNF180
ENST00000224862	0.0234	0.001	−4.54844	0.000707	FBXL15
ENST00000225275	1.8012	3.7582	1.061083	4.22E-05	MPO
ENST00000230173	0.001	0.0062	2.632268	0.00066	ADGRG6
ENST00000230990	2.3934	5.1126	1.094996	0.000229	HBEGF
ENST00000231173	0.0012	0.009	2.906891	0.000221	PCDHB15
ENST00000231751	0.2456	0.623	1.342922	0.001308	LTF
ENST00000232424	0.1168	0.4342	1.894319	2.58E-08	HES1
ENST00000233714	0.001	0.0276	4.786596	0.001496	LANCL1
ENST00000233997	1.5778	3.3686	1.094235	0.000295	AZU1
ENST00000236826	1.054	3.4208	1.698459	3.56E-07	MMP8
ENST00000237264	0.001	0.0462	5.529821	2.69E-07	TBPL1
ENST00000238508	0.1864	0.5244	1.492266	0.000341	SERPINB10
ENST00000239316	0.0026	0.0172	2.725825	0.000322	INSL4
ENST00000239938	35.003	138.1178	1.980349	1.06E-08	EGR1
ENST00000241356	0.8688	1.8864	1.11854	9.38E-06	ADORA3
ENST00000242208	0.082	0.3154	1.943487	2.64E-10	INHBA
ENST00000242480	0.8694	2.736	1.653976	7.11E-08	EGR2
ENST00000242737	2.8472	1.0502	−1.43888	0.000686	ITPR2
ENST00000244050	0.3902	0.9026	1.209873	0.000287	SNAI1
ENST00000244336	2.7612	7.5754	1.456027	2.50E-06	CEACAM8
ENST00000244364	0.0102	0.001	−3.3505	2.04E-06	DST
ENST00000252675	0.0456	0.1404	1.622437	3.31E-05	FUT5
ENST00000253408	0.0088	0.0636	2.853451	0.000537	GFAP
ENST00000255427	0.0126	0.0916	2.861924	0.000663	CHIT1
ENST00000257264	2.2706	5.1756	1.188653	1.84E-10	TCN1
ENST00000258400	0.001	0.0108	3.432959	0.000351	HTR2B
ENST00000258494	0.001	0.0076	2.925999	7.91E-05	ALDH1L2

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000258963	3.2004	6.5878	1.041545	0.000937	VEZF1
ENST00000259206	0.0306	0.001	−4.93546	0.000568	IL1RN
ENST00000259951	0.0736	0.0034	−4.4361	0.000871	HLA-F
ENST00000261944	0.001	0.0094	3.232661	0.000368	CDHR2
ENST00000262304	0.013	0.001	−3.70044	7.49E-06	PKD1
ENST00000262809	0.7448	1.837	1.302427	0.000152	ELL
ENST00000262865	3.837	7.9572	1.052282	5.32E-05	BPI
ENST00000263045	1.6118	4.4596	1.468242	3.68E-09	CRISP3
ENST00000263341	16.5414	43.6896	1.401209	2.67E-12	IL1B
ENST00000263545	0.001	0.0358	5.161888	8.82E-05	LUC7L2
ENST00000263621	1.157	2.7144	1.230244	5.73E-05	ELANE
ENST00000263707	0.067	0.002	−5.06609	4.20E-05	TFCP2L1
ENST00000264156	0.0116	0.3634	4.969362	5.28E-07	MCM6
ENST00000264498	0.001	0.0062	2.632268	0.000744	FGF2
ENST00000264956	0.0154	0.001	−3.94486	4.17E-05	EVC
ENST00000265881	0.1112	0.001	−6.79701	3.41E-05	REXO2
ENST00000265990	0.096	0.0124	−2.95269	1.45E-09	BTAF1
ENST00000273063	0.0136	0.001	−3.76553	7.83E-05	SLC4A3
ENST00000273077	0.001	0.0144	3.847997	0.001435	PNKD
ENST00000273347	0.1102	0.2382	1.112049	0.000991	NXPE3
ENST00000274710	0.0096	0.001	−3.26303	0.000112	PSD2
ENST00000277480	6.1284	15.075	1.298576	0.000139	LCN2
ENST00000278175	4.0576	9.7064	1.25831	9.36E-07	ADM
ENST00000278590	0.005	0.001	−2.32193	0.001398	ZC3H12C
ENST00000278756	4.8168	10.7066	1.152353	0.001103	APLP2
ENST00000278865	2.041	4.6692	1.193899	1.80E-07	MS4A3
ENST00000282120	0.0408	0.001	−5.3505	3.96E-06	TGOLN2
ENST00000282282	0.1732	0.3508	1.01821	5.87E-06	ZNF547
ENST00000283426	0.0212	0.0044	−2.26849	0.001026	PLEKHG4B
ENST00000284551	0.9296	2.254	1.277806	1.59E-06	TRIM11
ENST00000286627	0.0096	0.001	−3.26303	7.95E-05	KCNMA1
ENST00000292169	0.3618	0.0032	−6.82098	6.20E-05	S100A1
ENST00000293662	0.331	0.8206	1.309848	4.16E-06	GRASP
ENST00000293677	0.001	0.0918	6.520422	3.14E-06	RAVER1
ENST00000294702	0.0106	0.001	−3.40599	0.001431	GFI1
ENST00000295992	0.0286	0.1144	2	0.000404	PCOLCE2
ENST00000296435	8.3026	17.1748	1.048658	5.01E-06	CAMP
ENST00000297239	0.0388	0.001	−5.27798	0.000112	SYTL3
ENST00000297435	2.3918	6.9666	1.542358	5.58E-06	DEFA4
ENST00000299502	0.3266	1.0236	1.648055	1.48E-06	SERPINB2
ENST00000299969	0.0292	0.008	−1.8679	0.000283	SERINC4
ENST00000300027	0.001	0.0152	3.925999	3.53E-05	FANCI
ENST00000301624	0.0006	0.119	7.631783	1.71E-06	TNRC6C
ENST00000301698	0.019	0.0024	−2.98489	0.000768	PRR25
ENST00000302035	0.0116	0.1026	3.144834	0.001254	SLAMF1
ENST00000302291	0.001	0.01	3.321928	0.000215	LUZP1
ENST00000302326	0.0614	0.1664	1.438345	0.000946	MN1
ENST00000302328	0.0024	0.0244	3.345775	0.000313	SCN11A
ENST00000302779	0.0414	0.001	−5.37156	0.000216	PXK
ENST00000303391	0.001	0.597	9.221587	1.02E-13	MECP2
ENST00000303562	122.7578	289.7258	1.238873	1.13E-07	FOS
ENST00000304639	1.7764	4.1508	1.224433	0.000958	RNASE3
ENST00000306061	1.0988	6.8182	2.633462	4.06E-17	MT1E
ENST00000306090	0.0032	0.2008	5.971544	0.000344	GNAS
ENST00000306151	0.0008	0.0346	5.434628	4.01E-05	MUC17

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000306585	0.001	0.016	4	0.001358	CHTF8
ENST00000307407	260.8124	576.8646	1.14522	1.53E-06	CXCL8
ENST00000307885	0.001	0.0096	3.263034	0.000155	ADCY6
ENST00000309539	0.2124	0.8638	2.023914	9.00E-06	OLR1
ENST00000309902	0.0422	0.001	−5.39917	8.46E-06	ZNF407
ENST00000312943	0.001	0.0882	6.462707	3.62E-06	DOK3
ENST00000317216	6.415	22.1836	1.789972	2.73E-09	EGR3
ENST00000317276	3.6124	8.6866	1.265834	2.47E-05	PER1
ENST00000317721	0.0048	0.001	−2.26303	0.000439	NCKAP5
ENST00000319397	18.132	8.0092	−1.17881	5.15E-09	ETS1
ENST00000322748	0.0032	0.0552	4.108524	0.000709	ZNF18
ENST00000323938	0.011	0.1666	3.920813	0.000919	LGALS8
ENST00000325094	0.0258	0.001	−4.6893	1.80E-05	TMEM33
ENST00000327857	31.7274	106.71	1.749894	9.79E-06	DEFA3
ENST00000330439	0.1554	2.5418	4.031792	8.71E-18	MT1E
ENST00000330862	0.0046	0.0522	3.504344	5.35E-06	TMEM89
ENST00000331224	0.008	0.0796	3.314697	0.000587	DLK1
ENST00000332904	0.207	0.0994	−1.05831	0.001385	CDHR1
ENST00000337532	0.084	0.001	−6.39232	1.85E-05	MPP7
ENST00000337843	0.0172	0.001	−4.10434	0.000386	C1QTNF6
ENST00000338183	0.001	0.023	4.523562	0.000193	C15orf41
ENST00000338962	0.3224	0.7634	1.243587	6.55E-11	LRP1
ENST00000339861	0.001	0.0292	4.867896	1.99E-06	SEMA4D
ENST00000340552	0.5436	0.024	−4.50144	0.000124	LIMK2
ENST00000340800	0.0516	0.001	−5.6893	4.78E-07	ACSL4
ENST00000340855	0.001	0.0092	3.201634	0.000583	IDS
ENST00000341671	0.0252	0.001	−4.65535	1.97E-05	LRRC37B
ENST00000341852	0.1028	0.0064	−4.00562	0.000818	TNIK
ENST00000341911	0.0206	0.0008	−4.6865	0.001394	MYB
ENST00000342579	0.1454	1.0296	2.823985	0.000996	BPTF
ENST00000343195	0.0122	0.086	2.817456	0.000125	KCNIP2
ENST00000344722	0.001	0.0224	4.485427	2.76E-05	SMC4
ENST00000344774	0.0256	0.0022	−3.54057	0.000298	FAM166A
ENST00000346330	0.0532	0.0018	−4.88536	0.000158	UBE2A
ENST00000346964	0.001	0.0464	5.536053	5.51E-06	DLG1
ENST00000347401	0.001	0.0044	2.137504	0.001491	COL6A3
ENST00000347471	0.0006	0.0272	5.5025	0.001259	SMARCC2
ENST00000350199	0.8082	1.771	1.13178	0.000665	RNF38
ENST00000350773	0.001	0.0092	3.201634	0.000568	TSC2
ENST00000352551	0.0008	0.0414	5.693487	0.000166	UBE2C
ENST00000352732	5.5954	13.9578	1.318758	3.88E-09	ABHD2
ENST00000353660	0.001	0.027	4.754888	0.000636	RBCK1
ENST00000355667	0.0576	0.001	−5.848	1.38E-05	DNM2
ENST00000355946	0.0062	0.001	−2.63227	0.000318	SH3PXD2A
ENST00000356249	0.001	0.008	3	0.000446	CEMIP
ENST00000356348	0.3538	0.7496	1.083187	0.000111	KPNA5
ENST00000356628	0.05	0.1298	1.37629	0.000832	NRARP
ENST00000357008	0.001	0.0166	4.053111	0.000103	CHD4
ENST00000357570	0.0246	0.001	−4.62059	6.71E-07	CACNA1E
ENST00000357702	0.0094	0.001	−3.23266	0.00129	SAP130
ENST00000357736	0.001	0.2582	8.012345	4.95E-10	MAFG
ENST00000358077	0.0016	0.0698	5.447083	0.000602	DAPK1
ENST00000358768	0.0136	0.0008	−4.08746	0.000292	PARD3B
ENST0000358791	0.0354	0.0002	−7.46761	4.40E-05	BCAS4
ENST00000358825	0.0144	0.001	−3.848	8.97E-05	PRDM10

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000359576	0.001	0.011	3.459432	0.000434	CLASP2
ENST00000359645	0.0418	0.0012	−5.1224	0.00031	MBP
ENST00000359671	0.001	0.008	3	0.000112	FN1
ENST00000359709	3.1242	6.2692	1.004795	0.000505	IFI16
ENST00000359972	0.001	0.0506	5.661065	2.45E-06	APAF1
ENST00000360289	0.0104	0.001	−3.37851	0.00091	HK1
ENST00000360997	0.0004	0.0084	4.392317	0.00041	FAM107A
ENST00000361690	3.569	7.8604	1.139083	0.000707	SRPK1
ENST00000366837	0.0202	0.001	−4.33628	0.001503	EPHX1
ENST00000367030	0.001	0.0098	3.292782	0.000144	LAMB3
ENST00000367084	0.001	0.029	4.857981	4.48E-06	YOD1
ENST00000367468	69.4708	156.7534	1.174018	2.66E-07	PTGS2
ENST00000367949	0.0294	0.001	−4.87774	5.37E-05	FCRLA
ENST00000368114	0.022	0.2212	3.329776	0.000973	FCER1A
ENST00000368285	0.033	0.001	−5.04439	2.58E-05	SEMA4A
ENST00000368286	0.0338	0.001	−5.07895	8.70E-05	SEMA4A
ENST00000368678	1.792	4.7582	1.408845	0.001159	FYN
ENST00000368682	0.001	0.2784	8.121015	3.77E-10	FYN
ENST00000368932	0.001	0.1176	6.877744	7.10E-07	CDC40
ENST00000369040	0.0284	0.001	−4.82782	3.96E-06	ATE1
ENST00000369298	0.0348	0.001	−5.12102	9.27E-05	PIAS3
ENST00000369733	0.0408	0.1026	1.33039	0.000542	COL17A1
ENST00000369915	0.001	0.0146	3.867896	0.001168	TKTL1
ENST00000370401	0.0088	0.001	−3.1375	0.000488	MAMLD1
ENST00000370924	0.098	0.2312	1.238288	0.000224	PTGER3
ENST00000371160	0.001	0.0166	4.053111	0.000108	STAG2
ENST00000371489	0.001	0.0184	4.201634	0.000805	MYOF
ENST00000372764	0.2062	0.969	2.232452	5.01E-11	PLAU
ENST00000373525	0.001	0.0146	3.867896	0.000491	ATG16L1
ENST00000374024	0.0044	0.0294	2.740241	0.000318	GPR3
ENST00000374848	0.0012	0.0436	5.183222	0.000259	TMEM246
ENST00000375053	0.001	0.0516	5.689299	7.01E-05	MAGED2
ENST00000375840	0.0446	0.0012	−5.21594	0.000996	STRADA
ENST00000377081	0.0082	0.001	−3.03562	0.000361	KIF1B
ENST00000377390	0.001	0.2122	7.729281	7.99E-07	SF1
ENST00000377877	2.8064	1.2408	−1.17745	0.001502	RNF38
ENST00000378239	0.001	0.1114	6.799605	5.65E-06	ERLEC1
ENST00000378569	0.001	0.1352	7.078951	3.51E-06	CCL7
ENST00000379016	0.001	0.0082	3.035624	0.00074	HIPK3
ENST00000379153	0.271	0.8604	1.666715	1.04E-05	CD83
ENST00000379254	3.0092	10.6272	1.82031	1.27E-06	SAT1
ENST00000379333	0.02	0.001	−4.32193	4.02E-05	SLC23A2
ENST00000379651	0.0454	0.0042	−3.43423	0.000604	MAP7D2
ENST00000379811	0.0298	0.926	4.957628	3.54E-07	MT1G
ENST00000380877	0.0876	0.201	1.198193	1.77E-05	GABPB1
ENST00000381309	0.0856	0.001	−6.41954	7.44E-07	KDM4C
ENST00000381497	0.001	0.0362	5.177918	0.001034	AC138969.1
ENST00000381573	0.0132	0.001	−3.72247	0.000699	CD274
ENST00000381923	0.027	0.0608	1.171112	0.001012	TMEM52B
ENST00000382111	0.0144	0.001	−3.848	0.000207	DEPDC5
ENST00000382542	0.0472	0.001	−5.56071	0.001266	GZMB
ENST00000382692	122.2304	289.618	1.244548	8.64E-05	DEFA1
ENST00000389169	0.001	0.0626	5.968091	1.75E-06	FLCN
ENST00000389282	0.001	0.022	4.459432	7.64E-05	WIZ
ENST00000389851	0.089	0.2336	1.392163	0.001061	UVSSA

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000391834	0.0216	0.001	−4.43296	0.000892	AKT1S1
ENST00000392746	0.037	0.0018	−4.36146	0.000621	RFX5
ENST00000392975	0.0282	0.001	−4.81762	0.000127	CYB561
ENST00000393001	0.0002	0.0748	8.546894	7.87E-06	AMMECR1L
ENST00000393041	0.0206	0.001	−4.36457	0.000322	BIN1
ENST00000393307	0.087	0.001	−6.44294	7.80E-07	RAB43
ENST00000393386	0.0002	0.0072	5.169925	6.39E-05	PTPRZ1
ENST00000393484	0.0116	0.196	4.078657	0.000943	TES
ENST00000394132	0.0068	0.001	−2.76553	0.001094	TTC23
ENST00000394479	2.4894	5.0416	1.018084	7.68E-07	REL
ENST00000394485	7.5228	16.8156	1.160459	2.99E-08	MT1X
ENST00000394611	0.001	0.0316	4.981853	2.04E-05	RTN4
ENST00000394649	0.0232	0.001	−4.53605	1.15E-05	MYO1D
ENST00000394713	0.0412	0.001	−5.36457	8.29E-07	LRRC37B
ENST00000394725	0.4972	1.123	1.17546	5.21E-07	SIAH1
ENST00000394904	0.001	0.024	4.584963	1.82E-05	SLC11A2
ENST00000395032	0.5426	1.2672	1.223683	0.00021	MS4A3
ENST00000395097	0.0016	0.3804	7.893302	5.05E-09	NR4A3
ENST00000395287	0.0424	0.001	−5.40599	1.35E-05	BRD2
ENST00000395392	0.0004	0.0296	6.209453	2.12E-06	KIF23
ENST00000395467	0.001	0.0236	4.560715	0.000405	ADAMTSL5
ENST00000395748	4.005	8.6518	1.111198	0.000558	AREG
ENST00000395989	0.0216	0.1538	2.831952	0.000414	ZFP64
ENST00000396200	0.0106	0.001	−3.40599	0.000676	PDP1
ENST00000396650	0.0622	0.2466	1.987186	0.001487	C15orf48
ENST00000397049	0.0574	0.001	−5.84298	0.000248	NUDT1
ENST00000397121	0.0008	0.0118	3.882643	0.00084	ZNF676
ENST00000397283	0.001	0.0324	5.017922	1.12E-06	ERMN
ENST00000398042	0.001	0.0252	4.655352	0.00024	TANGO2
ENST00000398246	0.2174	0.5198	1.257605	8.55E-08	LONRF1
ENST00000398499	0.001	0.049	5.61471	3.92E-07	ZBTB21
ENST00000398905	0.031	0.1174	1.921092	0.001283	ERG
ENST00000398907	0.006	0.001	−2.58496	0.00126	ERG
ENST00000399169	0.0228	0.001	−4.51096	6.10E-05	STOX1
ENST00000399839	0.001	0.0168	4.070389	0.000379	ADA2
ENST00000399975	0.001	0.0944	6.560715	2.72E-07	USP16
ENST00000400202	0.0072	0.001	−2.848	0.000623	NRIP1
ENST00000400566	13.5744	28.7188	1.081107	2.36E-14	SAMSN1
ENST00000401931	11.6478	36.344	1.64166	4.94E-07	CXCL8
ENST00000403870	0.001	0.0168	4.070389	0.000606	CCNJ
ENST00000405636	0.001	0.1964	7.617651	4.58E-06	TOMM40
ENST00000406998	2.4486	1.1584	−1.07982	6.03E-05	BACH2
ENST00000407218	0.0008	0.0462	5.851749	0.00017	MECP2
ENST00000407322	0.031	0.001	−4.9542	0.000925	RGS6
ENST00000409198	0.001	0.0022	1.137504	0.001363	NEB
ENST00000409417	0.001	0.0494	5.626439	0.000358	PDLIM2
ENST00000409588	0.0002	0.027	7.076816	7.12E-05	NIF3L1
ENST00000409787	0.001	0.0578	5.852998	0.000436	NT5C3A
ENST00000409917	0.1768	0.0146	−3.59808	0.000336	INO80B
ENST00000410034	0.001	0.0836	6.385431	1.45E-05	ANKZF1
ENST00000411732	0.0066	0.0812	3.620942	0.000329	EGR2
ENST00000412359	0.0148	0.001	−3.88753	0.000514	BUB1B
ENST00000412504	2.2868	1.0012	−1.1916	1.16E-10	IL1RAP
ENST0000412734	0.1042	0.007	−3.89586	0.000954	GET4
ENST00000413393	0.001	0.0732	6.193772	4.20E-06	MAPRE2

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000413636	0.7148	3.4676	2.278326	0.000724	CIRBP
ENST00000413724	1.8446	3.7196	1.011839	2.21E-06	MAP3K8
ENST00000414217	0.011	0.001	−3.45943	0.000328	PPIP5K2
ENST00000414248	0.001	0.0742	6.213347	1.40E-05	FES
ENST00000415603	0.8546	0.2186	−1.96696	0.00021	DHX16
ENST00000416658	0.033	0.357	3.435386	0.001058	SLMAP
ENST00000417439	1.0032	5.0328	2.326752	6.76E-05	LTF
ENST00000418259	0.001	0.016	4	0.000205	ATG2A
ENST00000418359	0.0004	0.328	9.67948	1.04E-08	CNOT2
ENST00000418561	0.001	0.1072	6.744161	7.83E-05	TTC17
ENST00000418622	0.0222	0.001	−4.47249	3.63E-05	RIC1
ENST00000419436	0.0006	0.0404	6.073249	0.000492	PAXIP1
ENST00000419948	1.8154	4.1536	1.194075	0.0007	HP1BP3
ENST00000420808	0.001	0.0644	6.008989	1.43E-05	NISCH
ENST00000421217	0.125	0.0006	−7.70275	0.000118	BCAP29
ENST00000422754	0.064	0.8278	3.693138	0.000281	IVNS1ABP
ENST00000424802	0.001	0.0416	5.378512	0.001222	QKI
ENST00000424834	0.001	0.0052	2.378512	0.000931	SPATA13
ENST00000425413	0.0388	0.001	−5.27798	8.54E-06	UBR4
ENST00000426455	0.001	0.0076	2.925999	0.00146	STAG3
ENST00000426532	8.2416	24.4034	1.566086	2.71E-06	LTF
ENST00000426880	0.2412	0.532	1.141196	0.001505	HRH4
ENST00000428637	0.023	0.1354	2.557522	0.000271	RAPH1
ENST00000428982	0.0128	0.001	−3.67807	0.000724	SYNGAP1
ENST00000429492	0.0026	0.043	4.047753	0.000353	OSBPL10
ENST00000430436	0.0324	0.001	−5.01792	2.25E-06	RALGAPA2
ENST00000431281	0.0176	0.001	−4.1375	0.00076	ACBD4
ENST00000431380	0.001	0.0286	4.837943	0.000645	SPON2
ENST00000431674	0.1392	0.4262	1.614371	2.60E-05	TBL1XR1
ENST00000432018	0.5166	1.365	1.401781	5.40E-05	IL1B
ENST00000432753	0.0752	0.001	−6.23266	0.000907	POR
ENST00000433368	0.004	0.0992	4.632268	0.000405	CRISP3
ENST00000435761	0.001	0.078	6.285402	1.39E-05	PSMD2
ENST00000435931	1.5656	3.9292	1.32752	7.71E-05	NABP1
ENST00000436757	0.001	0.2208	7.786596	1.11E-09	PITPNM1
ENST00000436863	12.846	5.579	−1.20324	2.46E-06	CASP1
ENST00000437626	0.0104	0.0002	−5.70044	0.000491	ADARB1
ENST00000437822	0.001	0.0266	4.733354	5.31E-05	TAF6
ENST00000438213	1.036	3.1064	1.58422	0.000695	CTSD
ENST00000439889	0.0364	0.001	−5.18587	0.000166	SIGLEC10
ENST00000441305	2.4346	1.1666	−1.06137	6.07E-05	RBM5
ENST00000442028	0.0118	0.001	−3.56071	0.000276	ABCB9
ENST00000442366	0.0826	0.001	−6.36807	1.53E-06	AIMP1
ENST00000442506	0.052	0.001	−5.70044	2.80E-06	NBAS
ENST00000443183	0.001	0.0384	5.263034	6.72E-06	DLG1
ENST00000444415	0.0048	0.0568	3.564785	0.000898	TRAF4
ENST00000444487	0.7756	2.0002	1.36676	9.40E-06	BCL3
ENST00000444533	1.3736	0.6516	−1.0759	6.11E-07	SSBP3
ENST00000444837	0.0386	2.2802	5.884416	1.91E-08	MT1G
ENST00000447379	0.001	0.0592	5.887525	0.000291	NEK6
ENST00000447485	0.0484	0.001	−5.59694	0.000584	ATP6AP2
ENST00000448077	0.003	0.0454	3.919658	0.001184	PPARD
ENST00000448100	0.1936	0.016	−3.59694	0.001476	ZGPAT
ENST00000449182	0.001	0.0136	3.765535	1.17E-05	PTPRZ1
ENST00000449406	0.001	0.0506	5.661065	0.000179	ST3GAL4

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000449416	1.2372	3.1574	1.351658	2.17E-10	ZNF331
ENST00000449627	2.5712	6.812	1.405637	0.000886	NFE2L2
ENST00000450232	0.2532	0.586	1.210623	7.48E-05	PFKFB3
ENST00000450926	0.0216	0.001	−4.43296	0.000979	INTS11
ENST00000451619	0.1024	0.2836	1.469642	0.000141	F13A1
ENST00000451956	0.0178	1.7578	6.62575	2.77E-05	GNAI2
ENST00000452463	0.001	0.0502	5.649615	0.000419	CREB3L2
ENST00000452696	0.0568	0.2382	2.068211	0.001317	DOT1L
ENST00000453873	0.0002	0.0174	6.442943	0.000669	KIAA1841
ENST00000453960	0.8178	0.2442	−1.74368	0.000906	MECP2
ENST00000454703	3.2506	7.0162	1.109984	5.54E-06	ACSL1
ENST00000455263	0.0166	0.001	−4.05311	0.000429	TP53
ENST00000456224	0.0216	0.0072	−1.58496	0.000857	SCN11A
ENST00000456990	0.001	0.1192	6.89724	7.58E-06	THEMIS2
ENST00000457296	0.001	0.0432	5.432959	0.001313	FGR
ENST00000457416	0.037	0.001	−5.20945	9.15E-05	FGFR2
ENST00000457692	0.0054	0.1254	4.537434	0.000295	SERPINB2
ENST00000457765	0.012	0.0014	−3.09954	0.000924	PLPPR4
ENST00000458278	0.071	0.0166	−2.09664	0.000839	ANKRD54
ENST00000458358	0.001	0.0186	4.217231	0.0003	ITGA6
ENST00000464465	12.5894	0.9218	−3.77161	0.000105	CSF3R
ENST00000464818	0.0458	0.001	−5.51728	0.000475	PRKCD
ENST00000465903	0.0544	0.0038	−3.83954	8.98E-05	SMC4
ENST00000466255	0.001	0.0442	5.465974	0.001456	SLMAP
ENST00000466335	0.0884	0.2028	1.197939	0.000394	HACD1
ENST00000466983	0.0734	0.1758	1.260083	0.001065	SLC25A25
ENST00000467517	0.0366	0.0072	−2.34577	0.00081	NOS3
ENST00000469075	0.001	0.0134	3.744161	0.001462	NVL
ENST00000470821	0.0912	0.0004	−7.83289	1.41E-05	ARMC8
ENST00000471298	0.001	0.0982	6.617651	6.22E-05	CEACAM1
ENST00000471855	0.119	3.9434	5.050407	0.000186	RPL36A
ENST00000471858	0.001	0.0334	5.061776	8.77E-06	CD200R1
ENST00000471951	3.2666	1.5126	−1.11076	7.45E-06	ZMYND8
ENST00000472590	1.5542	3.3256	1.097442	6.03E-05	HHEX
ENST00000489157	8.3084	4.1198	−1.012	0.000851	TAPBP
ENST00000490703	0.1034	0.0066	−3.96963	0.00065	TBC1D10B
ENST00000492950	0.0294	0.001	−4.87774	0.00102	USP21
ENST00000494383	0.02	0.001	−4.32193	0.000266	AC097637.1
ENST00000503683	0.2528	0.0056	−5.49643	1.45E-06	SEC24D
ENST00000503860	0.0376	0.0054	−2.7997	0.000712	CXCL11
ENST00000504148	0.114	0.001	−6.83289	7.13E-05	TIMM8B
ENST00000504228	0.024	0.002	−3.58496	0.001061	KIAA1211
ENST00000504342	0.001	0.0252	4.655352	0.000247	ACSL1
ENST00000507661	0.1578	0.0454	−1.79733	0.000477	ARHGAP10
ENST00000508487	0.1572	0.532	1.758825	1.38E-05	CXCL2
ENST00000509047	0.0426	0.2188	2.360687	0.00013	ZNF331
ENST00000509570	0.0788	0.001	−6.30012	0.000236	SELENOW
ENST00000510624	0.001	0.0742	6.213347	0.000147	LEF1
ENST00000510911	0.037	0.0042	−3.13906	0.001388	FGFR4
ENST00000511481	0.068	0.5106	2.908587	0.001063	SEC24D
ENST00000512172	2.2486	1.1202	−1.00527	0.000636	LEF1
ENST00000512387	2.2552	5.118	1.182325	0.000219	ZNF331
ENST00000512470	0.0342	0.001	−5.09592	0.001384	SLC41A3
ENST00000512778	0.001	0.0886	6.469235	0.000221	SEPTIN11
ENST00000513042	0.001	0.0132	3.722466	0.000103	ARHGEF28

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000513137	0.0036	0.0174	2.273018	0.000978	SEMA6A
ENST00000513795	0.0022	0.1	5.506353	0.000119	SPDL1
ENST00000513826	0.001	0.0618	5.949535	3.42E-06	FBXO38
ENST00000514970	0.001	0.236	7.882643	8.76E-06	AFF1
ENST00000515359	0.0134	0.001	−3.74416	0.00024	DAG1
ENST00000515524	0.0034	0.0796	4.549162	0.000818	NSA2
ENST00000515735	0.1588	0.0366	−2.1173	0.000405	NSD1
ENST00000517649	0.001	0.0306	4.93546	2.48E-05	NAIP
ENST00000518977	0.8398	0.0586	−3.84107	0.000743	TNIP1
ENST00000519940	0.001	0.056	5.807355	2.40E-05	CARD8
ENST00000520223	0.001	0.0388	5.277985	0.001191	GPAT4
ENST00000520309	0.0154	0.001	−3.94486	0.000304	ANKAR
ENST00000520356	0.001	0.0486	5.602884	1.06E-06	ZFAT
ENST00000520986	0.0412	0.6888	4.063369	0.000338	DENND3
ENST00000522100	0.001	0.4874	8.928962	1.98E-07	TNIP1
ENST00000523149	1.197	0.4168	−1.522	0.001372	EXTL3
ENST00000525042	0.0452	0.001	−5.49825	0.000753	LGALS8
ENST00000525809	0.001	0.0368	5.201634	0.000876	BBS1
ENST00000525919	2.132	0.9952	−1.09915	0.000944	EMSY
ENST00000526014	0.001	0.0166	4.053111	0.00133	FXYD6
ENST00000526285	0.001	0.0404	5.336283	0.000729	GRK2
ENST00000527344	12.5394	5.6772	−1.14322	6.96E-06	CFL1
ENST00000527659	0.001	0.0218	4.446256	0.000322	EPB41L2
ENST00000528615	0.044	0.001	−5.45943	1.48E-05	DGKZ
ENST00000529318	0.0228	0.001	−4.51096	0.000514	SAAL1
ENST00000529447	0.5138	0.2184	−1.23423	0.000414	ZDHHC5
ENST00000531445	0.0096	0.0004	−4.58496	0.000749	C4orf50
ENST00000532057	0.098	0.627	2.677612	0.000144	FBXO3
ENST00000532463	0.001	0.0212	4.405992	7.03E-06	CTNND1
ENST00000532702	29.7676	65.1756	1.130589	8.77E-09	RPL8
ENST00000532703	0.001	0.0704	6.137504	0.000488	PITPNM1
ENST00000532846	0.0106	0.0492	2.214594	0.001415	RECQL4
ENST00000533129	0.001	0.158	7.303781	1.43E-06	CAPN1
ENST00000534247	0.2926	0.0252	−3.53743	8.49E-05	ZHX2
ENST00000536108	0.014	0.001	−3.80735	0.000533	KDM4C
ENST00000537194	0.0394	0.4072	3.36947	0.000208	SMAD3
ENST00000537561	0.001	0.0134	3.744161	0.000225	NUDT16
ENST00000537562	0.0004	0.0152	5.247928	0.000579	AMN1
ENST00000537750	0.0072	0.137	4.250035	0.001144	SYNE1
ENST00000537817	0.2318	0.0948	−1.28992	0.001488	C12orf43
ENST00000538384	1.4048	0.5874	−1.25795	0.00016	NOL10
ENST00000538577	0.001	0.0372	5.217231	0.00029	SLC35B2
ENST00000539661	0.001	0.03	4.906891	0.000294	RAB40C
ENST00000540264	0.534	1.1212	1.070132	0.000316	NFE2
ENST00000540338	0.001	0.0204	4.350497	7.49E-05	CLIP1
ENST00000540510	0.001	0.0348	5.121015	4.19E-05	GPR19
ENST00000540933	0.0224	0.001	−4.48543	4.08E-05	GANAB
ENST00000541043	0.001	0.0336	5.070389	4.85E-05	ACO1
ENST00000541102	0.165	0.002	−6.36632	4.83E-06	LTBR
ENST00000541951	0.0324	0.001	−5.01792	0.000645	PAAF1
ENST00000542120	0.0274	0.001	−4.7761	4.72E-06	TBC1D30
ENST00000544017	0.001	0.0202	4.336283	0.00028	TIMM50
ENST00000544327	0.0254	0.1286	2.33999	0.000982	SCARB1
ENST00000544484	0.001	0.0126	3.655352	6.22E-05	CHD4
ENST00000544971	0.0272	0.0016	−4.08746	7.14E-05	TRPV4

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ENST00000545872	0.119	0.001	−6.89482	2.49E-07	ZNF83
ENST00000547708	37.8826	18.019	−1.07202	0.000121	HNRNPA1
ENST00000548839	0.5064	1.824	1.848756	2.49E-09	LYZ
ENST00000550299	1.36	6.5598	2.270045	2.28E-05	PPP1R12A
ENST00000550716	0.7612	1.676	1.138675	0.000165	ATP2B1
ENST00000551457	3.2292	9.1232	1.498363	8.11E-10	TMCC3
ENST00000552244	0.05	0.359	2.843984	0.000937	RNF41
ENST00000552496	0.001	0.1098	6.778734	0.000361	CDK17
ENST00000554144	0.001	0.0132	3.722466	0.001031	HOPX
ENST00000554174	0.1876	0.4072	1.118078	4.44E-06	LRP1
ENST00000555672	83.829	38.2274	−1.13284	0.000337	FOS
ENST00000556134	0.001	0.018	4.169925	7.57E-06	KIAA0586
ENST00000556994	0.0208	0.001	−4.37851	0.000901	SRP54
ENST00000558373	0.001	0.0208	4.378512	0.000187	CTDSPL2
ENST00000558968	0.696	0.336	−1.05063	0.000949	CTDSPL2
ENST00000560177	0.001	0.0378	5.240314	8.70E-07	NUSAP1
ENST00000560338	0.397	1.4782	1.896631	0.001011	EIF5
ENST00000560520	0.0446	0.0008	−5.8009	0.000433	ICE2
ENST00000560521	0.1708	0.6464	1.920119	0.000464	RABGGTA
ENST00000561212	0.001	0.0308	4.944858	0.000581	ZEB1
ENST00000561491	0.8696	7.0584	3.020917	4.50E-12	MT2A
ENST00000562939	0.2528	2.0322	3.006974	1.16E-13	MT1X
ENST00000563402	0.2108	0.001	−7.71973	2.13E-06	MAZ
ENST00000563987	0.001	0.5306	9.051481	1.91E-06	ALDOA
ENST00000564003	0.001	0.054	5.754888	5.63E-05	MPI
ENST00000566419	0.0514	0.001	−5.6837	0.001194	NTAN1
ENST00000566742	0.2954	0.0668	−2.14475	0.000702	JPT2
ENST00000566946	0.0678	0.001	−6.08321	2.87E-05	ATXN2L
ENST00000567481	0.1732	0.0652	−1.4095	0.00095	ZFP1
ENST00000567887	0.001	0.0028	1.485427	0.00048	MACF1
ENST00000568293	0.0752	0.9304	3.629047	3.34E-07	MT1E
ENST00000568675	0.001	0.106	6.72792	1.85E-06	MT1G
ENST00000569155	0.001	0.0356	5.153805	0.000262	MT1H
ENST00000569500	0.0042	0.3174	6.239769	1.56E-06	MT1G
ENST00000575842	2.7222	8.4102	1.627367	9.08E-12	ACTG1
ENST00000576965	0.001	0.1454	7.183883	0.00012	RNF167
ENST00000577040	0.2602	0.0266	−3.29012	0.000167	GPS2
ENST00000579624	0.0492	0.001	−5.62059	0.000554	CNDP2
ENST00000580070	26.092	13.0098	−1.00401	0.001288	NCOA4
ENST00000581552	0.001	0.027	4.754888	0.000297	PIK3R5
ENST00000582117	0.0238	0.2492	3.388271	0.000107	LRRC37B
ENST00000584114	0.0028	0.1546	5.78697	0.000904	WSB1
ENST00000584650	0.02	0.001	−4.32193	0.001088	ELAC2
ENST00000585194	0.0862	0.001	−6.42962	7.64E-06	ZNF286A
ENST00000587615	0.0982	0.0118	−3.05694	0.001018	UBALD1
ENST00000588735	0.0014	0.0086	2.61891	0.00112	GFAP
ENST00000588982	0.0088	0.001	−3.1375	0.000927	ZBTB7C
ENST00000589377	0.0004	0.0092	4.523562	0.000909	KCNJ16
ENST00000589629	0.0012	0.1034	6.429058	0.000392	CDC37
ENST00000589640	0.3442	0.0236	−3.86639	0.000498	GPI
ENST00000589881	0.001	0.0154	3.944858	9.67E-05	ZNF24
ENST00000590414	0.001	0.0302	4.916477	0.000643	ZNF573
ENST00000590935	0.0178	0.001	−4.15381	0.000365	DUSP3
ENST0000591768	0.2142	0.0168	−3.67243	0.000201	USP32
ENST00000591811	0.404	0.1552	−1.38023	5.67E-05	CANT1

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ENST00000592282	0.0056	0.001	−2.48543	0.001412	ZNF260
ENST00000593591	0.0726	0.0016	−5.50383	0.000306	SH3GL1
ENST00000594442	0.001	0.1102	6.78398	2.60E-05	ZFP36
ENST00000594517	0.2572	0.1012	−1.34568	0.000295	ZNF677
ENST00000595618	0.001	0.0382	5.255501	7.91E-06	MYO9B
ENST00000596544	0.2146	1.6754	2.964784	0.001286	CEACAM3
ENST00000596853	0.319	2.1026	2.720546	0.000554	DNAJB1
ENST00000596894	0.0004	0.0306	6.257388	0.000248	ZNF546
ENST00000598915	0.0198	0.0002	−6.62936	0.000546	NAPSA
ENST00000599359	0.001	0.0826	6.36807	3.77E-06	TNFSF14
ENST00000599806	0.001	0.0284	4.827819	0.000404	VAV1
ENST00000600909	0.305	0.6274	1.040576	1.00E-05	KCNN4
ENST00000603300	0.0062	0.0206	1.732304	0.000727	DUOX2
ENST00000606731	0.8274	0.3442	−1.26534	1.50E-05	HOMEZ
ENST00000610538	0.0166	0.001	−4.05311	0.000429	TP53
ENST00000610640	0.001	0.0672	6.070389	0.000107	BTNL8
ENST00000610724	0.0248	0.0004	−5.9542	4.87E-05	TBL2
ENST00000610831	0.001	0.061	5.930737	5.27E-06	CARHSP1
ENST00000611646	0.016	0.001	−4	1.77E-05	RNF38
ENST00000611707	0.032	0.001	−5	0.000163	GPAT3
ENST00000612895	0.001	0.0086	3.104337	8.80E-05	ACACA
ENST00000613058	0.025	0.001	−4.64386	0.000301	SLC4A1AP
ENST00000613071	0.001	0.0122	3.608809	0.000425	TDRP
ENST00000613104	0.1144	0.5906	2.368094	3.64E-05	ATF3
ENST00000613273	0.0612	0.001	−5.93546	2.13E-05	TMEM185A
ENST00000613315	0.0042	0.1454	5.113494	0.000215	UBAP2L
ENST00000614035	0.001	0.5596	9.128252	2.46E-08	TNFAIP3
ENST00000614134	0.001	0.0068	2.765535	0.000529	JRK
ENST00000614382	0.1376	0.0166	−3.05123	3.84E-08	LFNG
ENST00000616144	0.2214	0.082	−1.43296	0.001005	BCL2L12
ENST00000616923	0.0424	0.001	−5.40599	2.70E-05	GCLC
ENST00000617249	0.001	0.022	4.459432	0.00107	PDIA6
ENST00000617706	0.026	0.001	−4.70044	0.000131	CBSL
ENST00000617859	0.0114	0.001	−3.51096	0.000702	IKZF5
ENST00000618040	0.001	0.0032	1.678072	0.000229	KCNN3
ENST00000618515	0.0286	0.001	−4.83794	1.67E-05	KIF3A
ENST00000618718	4.2948	1.8492	−1.21569	0.00099	CITED2
ENST00000618741	0.001	0.0524	5.711495	7.82E-06	LYPLA1
ENST00000618765	1.698	0.583	−1.54227	0.000248	RRP12
ENST00000619321	0.001	0.0438	5.452859	0.000148	SLC16A3
ENST00000619572	0.0024	0.1014	5.400879	0.000254	FAM214A
ENST00000619580	0.001	0.0456	5.510962	0.001259	PTMS
ENST00000619595	0.3864	0.8364	1.114098	0.000668	SERPINB10
ENST00000620047	0.0652	0.001	−6.0268	0.000619	PPIA
ENST00000620100	0.001	0.0172	4.104337	0.000131	STAG3
ENST00000620374	0.001	0.0224	4.485427	0.000106	ZNF195
ENST00000620571	0.001	0.015	3.906891	0.000113	MGAM
ENST00000621226	0.0002	0.004	4.321928	0.000803	MUC5AC
ENST00000621537	0.0664	0.001	−6.05311	7.61E-07	CMIP
ENST00000622396	0.0402	0.2478	2.623909	0.001249	TBKBP1
ENST00000625924	0.038	0.001	−5.24793	0.000827	RUNX2
ENST00000627059	0.0996	0.0116	−3.10202	0.001199	ALDOA
ENST00000627621	0.0966	0.8118	3.071029	0.000682	NFAT5
ENST00000629272	0.0252	0.001	−4.65535	0.001174	ATL2

ID	Control_fpkm	SZ_fpkm	log2(FC)	P value	Symbol
ENST00000629371	0.001	0.0194	4.277985	8.43E-05	AK2
ENST00000629688	0.0008	0.092	6.84549	0.000992	DRG1
ENST00000635833	0.001	0.036	5.169925	0.000121	RGS9
ENST00000636347	0.0182	0.001	−4.18587	9.83E-05	SLC9A6
ENST00000636941	0.001	0.013	3.70044	0.001408	TCAF2C
ENST00000637581	0.0148	0.001	−3.88753	0.000361	SLC9A6
ENST00000638375	0.001	0.0694	6.116864	0.000359	HLA-A
ENST00000638451	0.0364	0.001	−5.18587	0.000245	LIAS
ENST00000638972	0.0138	0.0002	−6.10852	0.000663	ADAMTS19
ENST00000639132	0.01	0.001	−3.32193	0.000903	BIVM-ERCC5
ENST00000639145	0.0158	0.001	−3.98185	0.000143	SCARB2
ENST00000640254	0.001	0.0134	3.744161	0.000711	STAT6
ENST00000642044	0.0258	0.001	−4.6893	0.000118	MICU1
ENST00000642248	0.001	0.029	4.857981	0.000295	CTNNB1
ENST00000643242	0.0094	0.001	−3.23266	0.001346	TCAF2
ENST00000643927	0.028	0.001	−4.80735	9.01E-06	PRKCB
ENST00000643977	0.001	0.0866	6.436295	2.38E-06	CTNNB1
ENST00000644774	0.138	0.001	−7.10852	3.03E-06	ACTG1
ENST00000644913	0.2388	0.065	−1.87729	0.001064	PLEKHG1
ENST00000644983	0.0974	0.3932	2.01327	0.000987	ALAS2
ENST00000645095	0.001	0.018	4.169925	0.000121	CHD4
ENST00000645632	0.001	0.08	6.321928	4.39E-08	VPS13A
ENST00000645988	0.0764	0.0088	−3.118	0.001439	DSE
ENST00000646168	0.001	0.0268	4.744161	0.00036	PRKCB
ENST00000646303	0.0236	0.001	−4.56071	9.59E-05	SPG7
ENST00000646369	0.001	0.0922	6.526695	1.62E-06	CTNNB1
ENST00000646646	0.0014	0.059	5.397216	0.00048	HSD17B4
ENST00000646649	0.001	0.0134	3.744161	1.31E-05	CUX1
ENST00000646673	0.0546	3.5362	6.017155	4.26E-07	SAMHD1
ENST00000647508	0.001	0.0226	4.498251	0.000398	SMARCE1

Supplementary Table 2. The score of Clinician-Rated Dimensions of Psychosis Symptom Severity scale

Sample	Disorganized Speech	Hallucination	Delusion	Abnormal psychomotor behavior	Negative symptom	Impaired cognition	Depression	Mania
Js 78	3	0	1	3	3	4	3	0
Js 70	2	1	3	3	0	3	0	2
Yx33	2	1	0	3	2	1	0	2
Yx23	2	2	3	2	0	3	0	2
Yx40	2	0	2	2	2	1	0	2
YX1	2	0	3	3	2	4	1	3
Yx34	2	2	2	2	0	1	0	2
Yx39	2	2	3	3	0	3	0	3
Yx47	2	0	1	3	2	3	0	0
Js 86	2	0	3	4	3	3	0	0
YX18	2	3	3	4	0	4	0	3
Js 81	2	2	2	2	0	1	0	0
JS31	0	1	3	3	3	3	0	0
Yx36	2	2	2	2	1	1	2	0

Sample	Disorganized Speech	Hallucination	Delusion	Abnormal psychomotor behavior	Negative symptom	Impaired cognition	Depression	Mania
Yx20	2	2	2	2	0	1	0	2
Js 67	2	3	3	0	0	4	0	3
Yx37	2	2	2	2	2	1	0	0
JS48	2	1	1	0	3	1	0	0
Yx25	2	2	2	3	0	1	2	0
JS33	3	0	1	3	3	4	1	0
JS19	2	1	3	0	0	1	0	0
YX2	3	0	3	3	0	4	0	3
YX4	0	3	1	2	2	1	0	0
JS40	2	2	2	2	0	1	2	2
YX15	3	2	4	3	0	4	0	3
YX8	2	3	3	3	2	4	0	0
Yx28	2	3	2	3	0	3	0	2
JS35	2	0	3	2	2	4	0	0
Yx21	2	0	1	2	2	1	0	2
JS55	0	2	3	2	0	1	0	0
JS32	2	2	2	0	0	1	0	0
JS2	2	0	1	2	2	0	1	0
JS4	2	0	3	0	3	4	0	0
Yx26	3	3	3	3	0	4	0	2
JS39	0	3	1	0	2	1	2	0
Yx42	2	0	3	2	2	4	0	1
Yx45	2	1	1	2	2	1	0	0
JS52	2	3	2	2	0	3	0	0
JS53	2	2	2	0	0	1	0	0
Js 66	2	2	2	2	0	1	0	0
JS25	2	2	1	0	2	1	0	0
Yx46	3	1	1	3	2	4	0	0
JS42	2	0	2	2	2	1	0	2
Yx49	3	3	3	4	0	4	0	0
JS37	2	2	2	0	0	1	2	0
JS22	2	1	2	0	0	1	0	0
JS41	2	2	3	0	2	3	1	0
JS38	2	0	2	2	2	3	1	0
JS50	2	1	4	3	0	4	0	3
JS27	2	0	3	3	2	3	1	0

Supplementary Table 3. WGCNA identified 89 risk genes related to abnormal psychomotor behavior characteristics in patients with schizophrenia.

IFI16, ETS1, BTAF1, LFNG, HHEX, ITPR2, MT1X, REL, RELT, NCOA4, SAMSN1, SIAH1, FBXO3, TAPBP, CTSD, GRASP, CXCL8, PTGS2, ACTG1, RNF38, HES1, ADM, PPP1R12A, FOS, SAT1, MAP3K8, FYN, NFE2L2, NRARP, DNAJB1, SNAI1, TBL1XR1, MN1, BCL3, CFL1, GABPB1, LONRF1, PLAU, ADORA3, SSBP3, F13A1, CD83, TRIM11, CITED2, IL1B, DUOX2, AREG, SERPINB2, CXCL2, VEZF1, PTGER3, FUT5, ABHD2, LEF1, TMCC3, HP1BP3, ZNF547, ATP2B1, NFE2, HBEGF, IL1RAP, ZNF331, PFKFB3, KPNA5, MT1E, LYZ, UVSSA, NXPE3, MT2A, PER1, EGR2, RBM5, HOMEZ, EGR3, BACH2, ZNF180, HRH4, EGR1, ATF3, NFAT5, PIN4, LRP1, ELL, ACSL1, EIF5, HNRNPA1, NABP1, CTDSPL2, CIRBP

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