

## Gene ontology analysis of obsessive-compulsive disorder related expressed genes

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### ABSTRACT

Obsessive-Compulsive Disorder is one of the complex mental disorders that combination of genetic components and environmental factors influence its phenotype. In this study, data from microarray findings has been evaluated from gene ontology perspective. The raw data from GEO was at first analyzed by the use of GEO2R Software as two groups of samples (Normal/OCD and Normal/ OCD with comorbidity); and then enrichment analysis of 50 significant differentially expressed genes of each group of samples was handled. The data indicates that enrichment findings in two groups are relatively similar. Furthermore, regulation of transcription, plasma membrane, and nucleotide and ion bindings are the most involved processes, parts and functions, respectively. In conclusion, these terms can be introduced as potential representations in OCD risk; however, clinical validations are required and suggested. Thus, for this aim, systematic molecular studies, particularly in the field of proteomics and metabolomics are fundamental.

**Keywords:** Obsessive-Compulsive Disorder, Gene ontology, Gene expression.

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### Introduction

Obsessive-compulsive disorder is a complex neuropsychiatric disorder that is typical with intrusive thoughts and repetitive acts. It was previously categorized as anxiety disorders, but in 2013, it was moved to a new section as “Obsessive and Compulsive and Related Disorders” by American Psychiatrist Association (1). lifetime prevalence of OCD is estimated about 1 to 3% around the world (2). Many different studies indicated that etiopathology of OCD is related to the various factors (3). Genetic and environmental factors combine and manifest different subtypes of

OCD (2). The main subtypes of OCD comprise of contamination/cleaning, checking, hoarding and rumination (4). Most of the OCD molecular studies are related to genetic basis of this disorder. Genetic foundation of OCD is very complicated as many genes with their polymorphism are linked to OCD risk (2, 5, 6). Numerous susceptibility parts of the genome are relevant to this familial disorder (7). This fact purpose OCD as a polygenic disease with many subtypes. Pathways of serotonin, dopamine, glutamate, and their communications are important in cortico-striatal circuits. In fact,

dysfunction in cortico-striatal-thalamo-cortical (CSTC) circuitry is the main incident in OCD pathophysiology (8). These include the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), thalamus and striatum (9). However, more research is needed to find out other implicated processes of this disorder for providing other treatment strategies. Many treatment options are available for OCD (10). One of the popular medicines is serotonin reuptake inhibitors (SRIs) family. However, not all the patients with OCD response to this type of drug family (11). The etiology of OCD has remained challenging over the past years since the manifest of this heterogenic disease is accompanied with different phenotypes that include overlap between OCD and other types of anxiety disorders including tic, phobia, and bipolarity (12). Molecular studies can be helpful to examine other potential agents in OCD nature and therefore can provide better treatment options. Bioinformatics is one of the new disciplines in today modern world (20). Its application is very wide that engaged with large dataset analysis. Gene ontology analysis showed promising role in presenting fundamental knowledge of massive molecular data (13). It comprises of three important features of biological process, molecular function and cellular component (14). The aim of this study is to provide characteristic information of the mRNA expression profiles of significant associated genes with OCD. In a way that, by the annotation analysis of the related gene products, a better insight in treatment options for OCD patients can be provided.

### Materials and Methods

The study of "*Genetic Neuropathology of Obsessive Psychiatric Syndromes*" by Jaffe AE et al(15), in 2014 was selected for gene ontology

evaluations. In this study, gene expression levels of different kinds of obsessions are studied from postmortem human brain dorsolateral prefrontal cortex (DLPFC) tissue. For this research, the gene expression data of OCD human samples and control ones from Gene Expression Omnibus (GEO) with series number of GSE60190 was extracted. The first analysis step was to compare the expression levels between control and OCD male samples. In this regard, GEO2R as a dataSet analysis tool was applied for differentially expressed genes analysis. By applying GEOquery and limma R packages from the Bioconductor project, GEO2R analyses the selected datasets (GDS) by using multiple-testing corrections based on P-values. In fact, it performs R statistical analysis independent of operator. The *Benjamini & Hochberg* (false discovery rate) is the applied P-value adjusted method. GEO2R provides statistical information including adjusted P. value, Raw P-value, B-statistic, Log 2-fold, moderated t-statistic and moderated F-statistic. Here the top genes are selected for further evaluations with  $p$ -value  $<0.05$ . Uniprot accession numbers for each gene were retrieved from Uniprot.org. The codes were applied for enrichment analysis using DAVID bioinformatics resources 6.7 (<http://david.abcc.ncifcrf.gov>) (16). Annotation cluster analysis by DAVID software can be helpful in retrieving genes related information based on different annotation aspects such as (GO) function category. In each clusters, the count numbers signify the number of annotated proteins for each mentioned term in DAVID output. Similar related biological features are grouped in individual clusters.

### Results

Comparison of gene expression profiles was performed between two samples of normal

(without psychiatric disorder) and OCD patients. For this purpose, two groups are defined as normal/OCD (group 1) and normal/OCD with comorbidity (group 2) and their gene expression

profiles were analyzed with GEO2R (See tables 1 and 2). The two groups were examined for gene ontology (BP, CC, MF) analysis. For each group, 50 top differentially expressed genes were selected.

**Table 1.** Gene expression profiles of group 1 (4 normal and 4 OCD patients) analyzed with GEO2R. The result is presented as a table of genes ordered by significant amounts (adj. P-Val <0.05 and P-value <0.05)

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
▶ILMN_1707958	0.99	0.00024	-7.11	1.1304	-0.0846	AES	amino-terminal enha...
▶ILMN_1860518	0.99	0.000275	-6.95	0.9934	-0.0997		
▶ILMN_1792607	0.99	0.000417	6.47	0.569	0.0677	OBP2A	odorant binding prot...
▶ILMN_1750940	0.99	0.000422	-6.46	0.5575	-0.0855	SLITRK1	SLIT and NTRK-like...
▶ILMN_1684704	0.99	0.000678	5.95	0.0704	0.0369		
▶ILMN_2370772	0.99	0.000832	5.74	-0.1419	0.4795	EIF4G1	eukaryotic translatio...
▶ILMN_1876703	0.99	0.001073	5.49	-0.4055	0.2678		
▶ILMN_2329958	0.99	0.001454	-5.2	-0.7219	-0.3782	ABI1	abl-interactor 1
▶ILMN_1914034	0.99	0.001501	-5.17	-0.755	-0.0398		
▶ILMN_2234515	0.99	0.001511	5.16	-0.762	0.3343	SLC7A5P2	solute carrier family ...
▶ILMN_1767184	0.99	0.001748	5.03	-0.9138	0.0577		
▶ILMN_1730796	0.99	0.002056	4.88	-1.0837	0.0367	NPHP1	nephronophthisis 1 (...)
▶ILMN_1756220	0.99	0.002209	-4.81	-1.1585	-0.3646	DDX18	DEAD (Asp-Glu-Ala-...
▶ILMN_1712031	0.99	0.002328	-4.77	-1.2134	-0.1472	SPDYE6	speedy/RINGO cell c...
▶ILMN_1779185	0.99	0.002528	4.69	-1.2999	0.3862	SPECC1L	sperm antigen with c...

**Table 2.** Gene expression profiles of group 2 (10 normal and 10 OCD patients with comorbidity) analyzed by GEO2R. The finding is presented as a table of genes ordered by significance (adj. P value <0.05 and P-value <0.05).

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
▶ILMN_1760089	0.0066	1.36e-07	-8.15	7.75578	-0.2289		
▶ILMN_1739154	0.0102	6.08e-07	7.35	6.27251	1.1186	LSAMP	limbic system-assoc...
▶ILMN_1802780	0.0102	7.01e-07	-7.28	6.13218	-0.3647	CD163L1	CD163 molecule-like 1
▶ILMN_2102515	0.0102	8.40e-07	-7.18	5.9528	-0.2829	PGAM4	phosphoglycerate m...
▶ILMN_1698406	0.0109	1.12e-06	7.04	5.67052	0.5418	ORMDL1	ORMDL sphingolipi...
▶ILMN_1860288	0.0198	2.44e-06	-6.65	4.89594	-0.5041	MBTPS2	membrane-bound tr...
▶ILMN_1904111	0.0274	3.94e-06	6.41	4.41899	0.1837		
▶ILMN_1685985	0.0275	4.55e-06	-6.34	4.27798	-0.1942		
▶ILMN_1813573	0.0275	5.37e-06	-6.26	4.11253	-0.1471	SETD1B	SET domain contai...
▶ILMN_2261784	0.0275	5.65e-06	-6.24	4.06281	-0.8431	CCNY	cyclin Y
▶ILMN_1696702	0.0316	7.13e-06	6.13	3.83034	0.4441	NEO1	neogenin 1
▶ILMN_1768558	0.0317	7.82e-06	-6.08	3.73946	-0.13		
▶ILMN_1690295	0.0352	9.40e-06	-6	3.55598	-0.3294		
▶ILMN_1729515	0.0382	1.10e-05	-5.92	3.40179	-0.291	PIN4	protein (peptidylprol...
▶ILMN_1848226	0.0397	1.22e-05	-5.87	3.29525	-0.0895		
▶ILMN_1781225	0.0495	1.74e-05	-5.71	2.94319	-0.3421		
▶ILMN_1678707	0.0495	1.80e-05	5.69	2.91033	0.7526	TAF15	TAF15 RNA polyme...
▶ILMN_1803742	0.0495	1.83e-05	-5.68	2.89376	-0.1964	CAPZA1	capping protein (acti...
▶ILMN_1810324	0.0504	2.10e-05	5.62	2.75624	0.1667	SGCB	sarcoglycan, beta (4...

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**Table 3.** Clustering based on biological process (BP) for 50 significant differentially expressed genes in A. Group 1 and B. Group 2, by the use of David Bioinformatics V.6.7.

**2 Cluster(s)** [Download File](#)

Annotation Cluster 1		Enrichment Score: 0.48			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">protein amino acid phosphorylation</a>	RT		4	2.2E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">phosphorylation</a>	RT		4	3.1E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">phosphorus metabolic process</a>	RT		4	4.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">phosphate metabolic process</a>	RT		4	4.3E-1	1.0E0
Annotation Cluster 2		Enrichment Score: 0.26			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of transcription, DNA-dependent</a>	RT		6	4.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of RNA metabolic process</a>	RT		6	4.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">response to organic substance</a>	RT		3	5.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of transcription from RNA polymerase II promoter</a>	RT		3	5.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of transcription</a>	RT		7	6.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">transcription</a>	RT		5	7.8E-1	1.0E0

A

**4 Cluster(s)** [Download File](#)

Annotation Cluster 1		Enrichment Score: 1.11			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">cytoskeleton organization</a>	RT		5	2.8E-2	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">actin cytoskeleton organization</a>	RT		3	1.2E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">actin filament-based process</a>	RT		3	1.3E-1	1.0E0
Annotation Cluster 2		Enrichment Score: 0.48			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">macromolecular complex assembly</a>	RT		4	2.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">macromolecular complex subunit organization</a>	RT		4	2.9E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">protein complex assembly</a>	RT		3	3.9E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">protein complex biogenesis</a>	RT		3	3.9E-1	1.0E0
Annotation Cluster 3		Enrichment Score: 0.19			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of apoptosis</a>	RT		3	6.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of programmed cell death</a>	RT		3	6.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of cell death</a>	RT		3	6.5E-1	1.0E0
Annotation Cluster 4		Enrichment Score: 0.14			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of transcription from RNA polymerase II promoter</a>	RT		3	5.8E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of transcription, DNA-dependent</a>	RT		5	7.1E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of transcription</a>	RT		7	7.2E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">regulation of RNA metabolic process</a>	RT		5	7.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_BP_FAT	<a href="#">transcription</a>	RT		4	9.3E-1	1.0E0

B

IDs with gene symbols are chosen for the enrichments (See tables 3, 4, 5).

## Discussion

Obsessive-compulsive Disorder as one of the complex mental disorders is prominent to study from molecular aspect. Many OCD molecular studies are focused on genetic basis of the disorder. In this study, a research conducted by *Jaffe AE et al* (15) in 2014 was chosen for the gene ontology analysis. That is, GO perspective

of the most significantly altered genes expression is examined. Two groups of normal/OCD and normal/OCD with comorbidity are defined in this research. The first group consists of normal people with no mental disorder and OCD samples that were not reported with any kinds of comorbidity. The second group is the normal people and OCD patients with different kinds of comorbidity. The related comorbidity are bipolar, tic and MDD. As it is shown in table1, none of the

**Table 4.** Clustering cell component (CC) for 50 significant differentially expressed genes in A. Group1 and B. Group2, by the use of David Bioinformatics V.6.7.

**3 Cluster(s)** [Download File](#)

Annotation Cluster 1		Enrichment Score: 0.43			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">plasma membrane part</a>	RT		10	6.0E-2	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">cell junction</a>	RT		4	1.2E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">integral to plasma membrane</a>	RT		4	5.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">plasma membrane</a>	RT		10	5.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intrinsic to plasma membrane</a>	RT		4	5.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">integral to membrane</a>	RT		10	9.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intrinsic to membrane</a>	RT		10	9.5E-1	1.0E0
Annotation Cluster 2		Enrichment Score: 0.2			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">membrane fraction</a>	RT		3	5.7E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">insoluble fraction</a>	RT		3	5.9E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">cell fraction</a>	RT		3	7.4E-1	1.0E0
Annotation Cluster 3		Enrichment Score: 0.1			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">nucleolus</a>	RT		3	4.9E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intracellular non-membrane-bounded organelle</a>	RT		6	7.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">non-membrane-bounded organelle</a>	RT		6	7.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">membrane-enclosed lumen</a>	RT		4	8.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">cytoskeleton</a>	RT		3	8.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">nuclear lumen</a>	RT		3	8.7E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intracellular organelle lumen</a>	RT		3	9.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">organelle lumen</a>	RT		3	9.4E-1	1.0E0

A

**3 Cluster(s)** [Download File](#)

Annotation Cluster 1		Enrichment Score: 0.93			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">non-membrane-bounded organelle</a>	RT		11	8.1E-2	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intracellular non-membrane-bounded organelle</a>	RT		11	8.1E-2	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">cytoskeleton</a>	RT		6	2.4E-1	1.0E0
Annotation Cluster 2		Enrichment Score: 0.3			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">nucleolus</a>	RT		4	2.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">nuclear lumen</a>	RT		5	4.7E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intracellular organelle lumen</a>	RT		5	6.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">organelle lumen</a>	RT		5	6.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">membrane-enclosed lumen</a>	RT		5	6.8E-1	1.0E0
Annotation Cluster 3		Enrichment Score: 0.06			Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">intrinsic to membrane</a>	RT		12	8.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">plasma membrane</a>	RT		8	8.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_CC_FAT	<a href="#">integral to membrane</a>	RT		11	8.9E-1	1.0E0

B

genes confirmed significant expression changes based on adjusted P-Value while in table2, about 19 genes are significant in this manner. The top 50 ranked genes with significant expression changes (Raw P-Value) were targeted for gene ontology evaluations. However, the genes that possess gene symbol were chosen for the analysis and the rest of them were discarded due to not providing identity for the evaluation. In other words, the top 50 IDs with gene symbols were the finalized

selections. David Bioinformatics analysis indicates that the differentially expressed genes in postmortem human brain dorsolateral prefrontal cortex (DLPFC) tissue are related to many cell parts, processes and functions in OCD. The most known biological processes in OCD pathophysiology are serotonergic, dopamine, glutamatergic pathways based on SNP studies (17, 18). Conversely, here, other involved processes are introduced. This is also confirmed by the Jaffe AE et al, that the

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**Table 5.** Clustering molecular function (MF) for 50 significant differentially expressed genes in **A.** Group1 and **B.** Group2, by the use of David Bioinformatics V.6.7.

**2 Cluster(s)** [Download File](#)

Annotation Cluster 1		Enrichment Score: 0.13		Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">nucleotide binding</a>	RT	6	7.0E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">ribonucleotide binding</a>	RT	5	7.1E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">purine ribonucleotide binding</a>	RT	5	7.1E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">purine nucleotide binding</a>	RT	5	7.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">ATP binding</a>	RT	4	7.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">adenyl ribonucleotide binding</a>	RT	4	7.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">adenyl nucleotide binding</a>	RT	4	7.8E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">purine nucleoside binding</a>	RT	4	7.9E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">nucleoside binding</a>	RT	4	8.0E-1	1.0E0
Annotation Cluster 2		Enrichment Score: 0.02		Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">cation binding</a>	RT	8	9.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">ion binding</a>	RT	8	9.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">zinc ion binding</a>	RT	4	9.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">metal ion binding</a>	RT	7	9.8E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">transition metal ion binding</a>	RT	4	9.8E-1	1.0E0

A

**3 Cluster(s)** [Download File](#)

Annotation Cluster 1		Enrichment Score: 0.93		Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">GTPase regulator activity</a>	RT	4	9.4E-2	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">nucleoside-triphosphatase regulator activity</a>	RT	4	9.9E-2	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">small GTPase regulator activity</a>	RT	3	1.7E-1	1.0E0
Annotation Cluster 2		Enrichment Score: 0.41		Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">zinc ion binding</a>	RT	9	2.8E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">transition metal ion binding</a>	RT	10	3.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">metal ion binding</a>	RT	13	4.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">cation binding</a>	RT	13	4.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">ion binding</a>	RT	13	4.8E-1	1.0E0
Annotation Cluster 3		Enrichment Score: 0.26		Count	P_Value	Benjamini
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">nucleotide binding</a>	RT	9	2.5E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">purine ribonucleotide binding</a>	RT	6	5.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">ribonucleotide binding</a>	RT	6	5.6E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">ATP binding</a>	RT	5	5.7E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">adenyl ribonucleotide binding</a>	RT	5	5.9E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">purine nucleotide binding</a>	RT	6	6.1E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">adenyl nucleotide binding</a>	RT	5	6.3E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">purine nucleoside binding</a>	RT	5	6.4E-1	1.0E0
<input type="checkbox"/>	GOTERM_MF_FAT	<a href="#">nucleoside binding</a>	RT	5	6.5E-1	1.0E0

B

involved expressed genes are totally different from previous introduced SNPs (15). The biological process (BP) enrichments of the 50 genes in samples of groups1 and 2 show that the involved genes in group2 are clustered in four groups, while in group1, genes are organized in two groups. The adjusted P-Value for clustering task is not significant, but the top processes are selected. The second finding indicates that, the related BP for the two

groups is different. For example, phosphorylation process is the most important process for the group1, but cytoskeletal organization is major one in group2. However, there are common processes such as transcription processes in the two groups. The analysis for CC terms shows more similarity for the two groups. The genes are clustered in the similar manner and the components are nearly alike. As it is depicted in table 5, despite,

difference between two groups from clustering aspects, it seems that the MF is very close for two groups.

In addition, regulation of transcription, plasma membrane, and nucleotide and ion bindings are the most involved processes, parts and functions, respectively. That is, these terms can be representing as the targets for investigating OCD treatment approaches. On the other hand, the different enrichment annotations between groups imply on the fact the possible differences are associated to the presence of comorbidity phenotypes. Our findings are consistent with the previous reported data that the clustering is useful tool for gene enrichment analysis (19). In the most bioinformatics researches, it is indicated that clinical studies are final and prominent approach for validating the theoretical assessments (20). Therefore, it is suggested that, the finding should be examined by other high-throughput screening tools.

## Conclusion

David bioinformatics analysis showed fine differences between OCD patients and the OCD patients with comorbidity in the gene expression level. In addition, this analysis provided additional molecular details for OCD phenotype and difference between OCD and OCD with comorbidity.

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*Expression Profile and Related SNPs via Bioinformatics and Orthogonal Tests*" project.

## Conflict of Interest

Not Declared.

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