Computational Pathway and Network Analysis of Gene Expression Data in L-DOPA-Induced Dyskinesia Models of Parkinson's Disease

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This study analyzed molecular changes that happen due to L-DOPA treatment in Parkinson's patients, using gene expression data from rats. When identifying genes that were differentially expressed, we saw correlations with cellular stress, neural transmission dysfunction, and different causes of inflammation. The pathway analysis highlighted processes such as endoplasmic reticulum stress, PI3K-Akt signaling, and circadian rhythm disruptions, which are known to be connected to L-DOPA-induced dyskinesia (LID). Finally, network analysis identified genes such as *CRY1* and *XBP1* as potential new regulators of all processes influenced by L-DOPA. These findings provide further evidence, based on previous studies, that *HSPA5*, a gene associated with cellular stress, may be a promising target for LID treatments.

1 INTRODUCTION

Parkinson's disease (PD) is a condition that results in the loss of neurons that affects 10 million people worldwide. This occurs because dopamine-producing neurons are lost in the *substantia nigra* [20]. While L-DOPA continues to be the main treatment choice to increase lost dopamine levels and improve motor abilities, its long-term use often leads to LID, a condition known for uncontrolled movements [30]. Understanding the molecular mechanisms that cause LID is important to help improve treatment and its impact on patients' lives.

LID occurs from a complicated interaction of factors, including dopamine receptor hypersensitivity, neurotransmitter imbalances, and cellular stress responses. Our study points to potential additional contributors, such as mitochondrial dysfunction, neurovascular remodeling, and circadian rhythm disruption. These changes affect neuronal homeostasis and increase the vulnerability of neurons to stress, potentially leading to the progression of dyskinesia.

Our study uses three different analysis methods, which are discussed later, to explore the molecular pathways involved in LID. Looking at key genes and their related processes, we examine how neurons respond to the challenges of long-term L-DOPA treatment and its potential impact on their performance.

2 MATERIALS AND METHODS

In this section, we introduce the resources which were used for the completion of this project. The dataset used in this study was taken from the Gene Expression Omnibus repository with the code GSE139438 [1, 3]. It consists of gene expression profiles from striata tissue from rats (lat. *rattus norvegicus*) treated with L-DOPA, and of untreated control rats. The treated groups were administered L-DOPA methyl ester and benserazide at doses of 25 mg/kg and 6.25 mg/kg. Both groups of rats have six subsets composed of 13375 samples, making the total size of the dataset 160500.

All R(v4.4.2) code was executed using RStudio version 2024.09.0+375.

The research explored three analyses:

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It begins with the **Differential Gene Expression Analysis (DGEA)**, performed using the `limma`(v3.60.6) [26] package in R, which applies linear modeling techniques to identify changes between the treated and control groups. The analysis is partly done using GEO2R and their visualization tools [1, 3].

The analysis identified genes that were significantly upregulated or downregulated due to L-DOPA treatment in Section 3.1. Gene selection was based solely on statistical significance using the adjusted p-value with a threshold of 0.05. The log2-fold change and t-statistic were included in the results for comparison but were not directly used for gene selection. All findings were supported by the visualizations provided by GEO2R.

After determining the most significant genes based on DGEA, the DGEA results were used as input to identify biological processes and diseases that could be linked to the symptoms of PD and LID in Section 3.2. This was achieved through **Pathway Enrichment Analysis (PEA)**, performed using the `clusterProfiler` (v4.12.6) package [32].

The methods and tools used for the PEA are outlined here:

- *Input Data:* Differentially Expressed Genes (DEG) with adjusted p-values below 0.05 were selected for analysis. This made sure that only genes with significant expression changes were included.
- *Pathway Databases:* Enrichment was carried out for Kyoto Encyclopedia of Genes and Genomes (KEGG) [21] pathways and Gene Ontology (GO) [4] terms. KEGG targets molecular pathways, while GO shows biological processes and molecular functions.
- *Parameters:* The analysis used default thresholds for enrichment significance, with a False Discovery Rate (FDR) cut-off of 0.05 and kept the pathways with all gene counts.
- *Visualization:* Significant pathways were visualized using dot plots to show their gene counts, adjusted p-values, and gene ratios. The visualizations were generated using the `clusterProfiler` (v4.12.6) [32], `enrichplot` (v1.24.4), and `plotly` (v4.10.4) [29] packages in R.

Lastly, the **Network Analysis (NA)** in Section 3.3 explored the interactions of DEGs identified in the study. This process involved combining differential expression data with gene interaction databases and running perturbation analyses to identify key nodes and interactions relevant to LID.

The NA consists of three main stages:

2.0.1 ***Mapping Differential Expression Statistics.*** Differential expression statistics, taken from a limma case-control analysis, were used to rank genes based on significance. Genes with adjusted p-values below 0.05 were selected for the analysis, and a total of 250 genes were used as input. This gene list was uploaded to the GeneGo MetaCore platform to construct a network based only on direct interactions. The following criteria were applied:

- *Object Types:* Excluded non-protein entities such as DNA, RNA, and metabolites.
- *Interaction Types:* Focused on transcription regulation, expression influence, and co-regulation of transcription with defined activating or inhibiting effects.

The resulting network files, including node mappings and interaction data, were exported in Excel format for the next steps.

2.0.2 ***Data Processing and Network Construction.*** The exported data was preprocessed in R to create input files for NA:

- *Node Mapping and Interactions:* Adjacency matrices were created to represent gene interactions, with missing interaction mechanisms inferred using an in-house developed script, as described in [33].

- *Expression Data Preparation:* Log2-fold changes were processed into binary formats (upregulated or downregulated) to allow perturbation modeling.

The processed data was visualized in Cytoscape (v3.10.3) [27], using hierarchical layouts. The colors of the nodes represented log2-fold changes to differentiate upregulated and downregulated genes.

2.0.3 ***Perturbation Analysis.*** Perturbation analyses were performed using Java-based tools:

- *Differential NA:* Compare the networks for treated and control conditions to identify changes in interactions caused by L-DOPA.
- *Cycle Detection and Stability Modeling:* Feedback loops were identified and their stability was analyzed under L-DOPA conditions.
- *Brute Force Perturbation:* Simulations were run to see what happens when individual genes are disrupted, helping to understand which genes are critical for network stability.

3 RESULTS

After examining the methods used in the analysis, we will now review the results findings by dedicating a section for each analysis.

3.1 Differential Gene Expression Analysis

The differential gene expression analysis was conducted to compare the treated group with the untreated control group, using the `limma` package in R. It revealed significant up- and down-regulation of genes, discussed in the following sections.

3.1.1 ***Upregulated Genes and Their Biological Implications.*** Several genes were significantly upregulated in the L-DOPA-treated group compared to the untreated group. Table 1 provides a summary of the key metrics for these genes.

Gene	Description	t-statistic	logFC	P.Value	adj.P.Val
HSPA5	Heat shock protein family A (Hsp70) member 5	15.52	0.80	5.92e-10	7.01e-06
ANGPT2	Angiopoietin 2	14.00	0.58	1.37e-09	7.01e-06
PLA1A	Phospholipase A1 Member A	14.21	0.72	1.82e-09	7.01e-06
PDYN	Prodynorphin	13.40	1.91	3.81e-09	1.02e-05

Table 1. Top upregulated genes and their metrics.

- **HSPA5** is a protein that helps maintain protein homeostasis by helping folding in the endoplasmic reticulum (ER). Its upregulation indicates cellular stress, possibly linked to the drug's effects on the brain [14].
- **ANGPT2** regulates angiogenesis and vascular remodeling and this way it influences blood vessel development. Its upregulation could imply changes in the brain's vascular function, potentially leading to an inflammatory reaction [12].
- **PLA1A** is involved in lipid metabolism. Its upregulation may suggest changes in lipid signaling pathways that could affect cellular processes [24].
- **PDYN** encodes a protein for several opioid peptides that influence synaptic plasticity. Its upregulation can interfere with opioid signaling, causing motor control problems, which can be seen in dyskinesia [23].

3.1.2 ***Downregulated Genes and Their Biological Implications.*** Genes that were significantly downregulated in the L-DOPA-treated group are summarized in Table 2.

Gene	Description	t-statistic	logFC	P.Value	adj.P.Val
ZBTB22	Zinc Finger And BTB Domain Containing 22	-11.35	-0.489	2.98e-08	3.98e-05
LYRM9	LYR Motif Containing 9	-10.28	-0.495	8.42e-08	1.10e-04
AMDHD2	Amidohydrolase Domain Containing 2	-9.12	-0.478	4.01e-07	2.20e-04

Table 2. Top downregulated genes and their metrics.

- **ZBTB22** regulates transcription and its downregulation may reduce the expression of genes involved in maintaining cellular stability. It could disrupt normal cell functions, making neurons more vulnerable to damage or stress, particularly during L-DOPA treatment [25].
- **LYRM9** is involved in mitochondrial function. Its downregulation suggests that mitochondrial activity may be compromised in response to L-DOPA treatment, potentially affecting energy production [18].
- **AMDHD2** encodes an enzyme involved in amino acid metabolism and its downregulation may imply disruptions in metabolic processes [17].

The distribution of the upregulated and downregulated genes can be found in Figure 1.

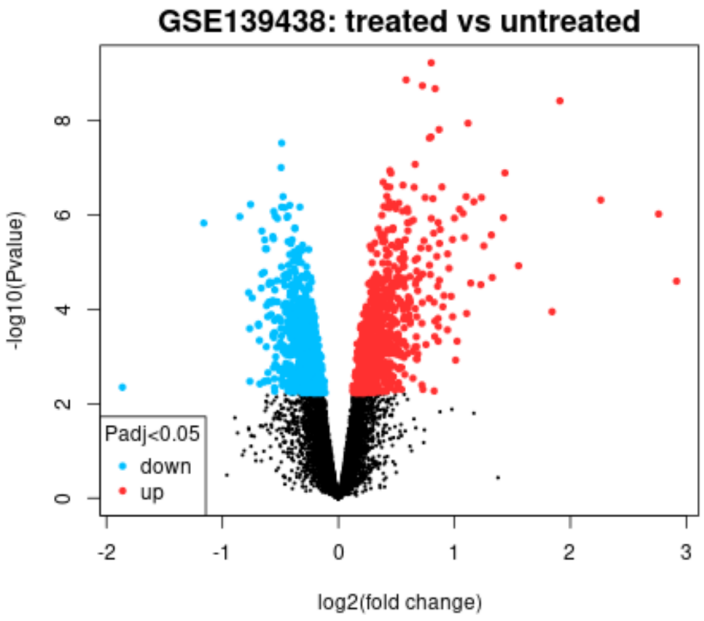

Fig. 1. Volcano plot showing upregulated (red) and downregulated (blue) genes in treated vs. untreated groups (adjusted p-value < 0.05).

3.2 Pathway Enrichment Analysis

The next analysis is the PEA, which identified several key KEGG pathways and GO terms. These pathways were closely related to cellular stress, inflammation, and metabolic adaptation. The results that provided this information are examined in the following sections.

3.2.1 ***KEGG Pathways.*** The KEGG analysis highlighted pathways associated with cellular stress, survival, and inflammation:

- *Protein Processing in the Endoplasmic Reticulum:* This pathway, involving genes such as *HSPA5*, *CALR*, and *XBP1*, highlight the role of ER stress in managing misfolded proteins and maintaining cell homeostasis under neurotoxic conditions [13, 14].
- *PI3K-Akt Signaling Pathway:* Genes such as *ANGPT2*, *VEGFA*, and *ITGA7* mapped to this pathway, which supports cell survival, stress response, and inflammation management. Its activation suggests that neurons may try to adapt to damage caused by L-DOPA [12].
- *Efferocytosis:* The involvement of *PPARD* and *CALR* suggests focus on clearing damaged or dying cells, helping to manage inflammation and oxidative stress[13].

Please refer to Figure 2 for the dot plot illustrating the most enriched pathways taken from the KEGG analysis.

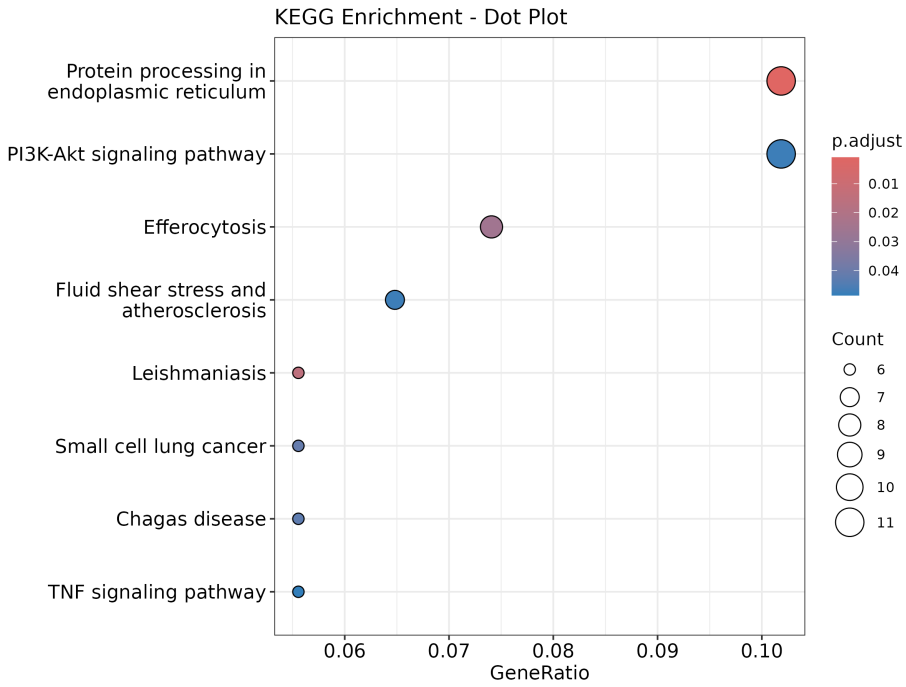

Fig. 2. KEGG enrichment analysis. Dot size indicates the gene count within each pathway, and the color gradient represents the adjusted p-value, with red representing higher values.

3.2.2 ***GO Biological Processes.*** The GO analysis revealed biological processes related to stress response, inflammation, and metabolic regulation:

- *Cellular Response to External Stimulus:* This category, enriched with genes such as *HSPA5* and *VEGFA*, highlights the response to neurotoxic stress and low oxygen levels (hypoxia), which has been known to be associated with brain disorders [22].
- *Regulation of Apoptotic Signaling Pathway:* Genes such as *MAP2K6* and *XBP1*, can contribute to an balance between survival and programmed cell death in neurons, which is important in neurodegeneration [16, 31].
- *Response to Endoplasmic Reticulum Stress:* This process, involving genes such as *HSPA5* and *CALR*, might reflects how ER stress plays a important role in the handling of damaged neurons [13, 14] .
- *Circadian Rhythm:* Although not traditionally linked to PD, the occurrence of genes like *CRY1*, *PTEN* and *KLF9* raises questions about the interaction between circadian regulation and neuronal health. A disruption of this pathway may affect different process like the regulation of cellular homeostasis, stress responses, and neuroinflammation [28].

Please refer to Figure 3 to see the dot plot of the GO enrichment analysis.

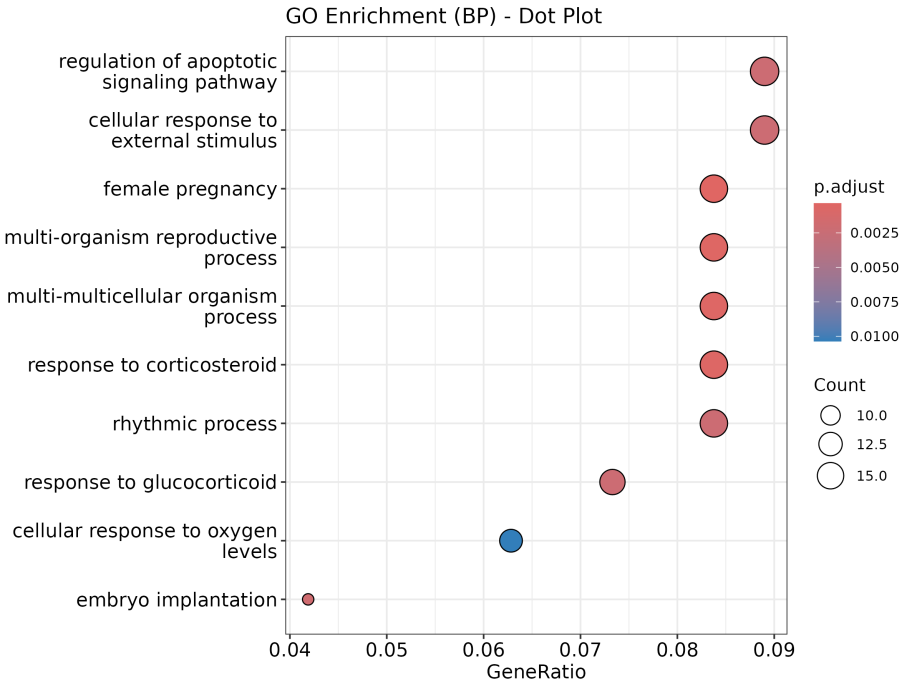

Fig. 3. GO enrichment analysis for Biological Processes. The size of the dots represents the number of genes involved in each process, while the color indicates the adjusted p-value, with red meaning higher values.

The PEA identified several reproductive pathways, such as *Female Pregnancy* and *Multi-Organism Reproductive Process* which are unlikely to be directly related to PD or LID. These findings likely stem from shared gene complexes, as certain genes involved in fundamental biological processes also play roles in the reproductive system. This is a common limitation of enrichment analysis. Multifunctional genes can be associated with pathways unrelated to the specific context of the study.

For example, the KEGG analysis of the *Protein Processing in the Endoplasmic Reticulum* and *Efferocytosis* pathways, as well as the GO analysis of the *Response to Endoplasmic Reticulum Stress* and various reproductive pathways, including *Female Pregnancy* and *Embryo Implantation*, has identified the presence of gene *CALR*. This finding connects it to both cellular stress in the ER and reproductive pathways, confirming that genes can overlap with different processes.

3.3 Network Analysis

To better understand the interaction of the genes present in our dataset, we implemented a network analysis. The results of this analysis were visualizations that represented the activating and inhibiting interactions. These interactions are listed and interpreted in the following subsections.

3.3.1 ***Visualization.*** The network visualization obtained with MetaCore was exported and then imported into Cytoscape for further visualization. Using Cytoscape, two networks were visualized:

- **Treated Group Network:** This network highlights the regulatory interactions and connectivity patterns specific to the treated group.
- **Control Group Network :** This network illustrates the regulatory interactions in the control group.

Figures 5 and 6 present the previously mentioned networks, with detailed legends that map the colors of the nodes to expression changes (see Figure 4). Edges are color-coded to represent interaction types in the networks in 5 and 6 : red indicates inhibitory interactions, and green represents activating interactions.

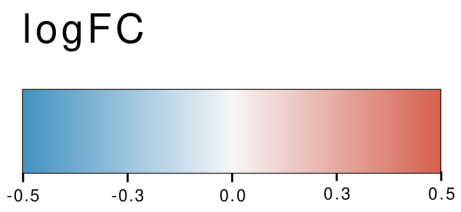

Fig. 4. Legend for log2-fold change of treated and control groups, showing gene expression changes. Blue indicates downregulated changes, while red indicates upregulated changes.

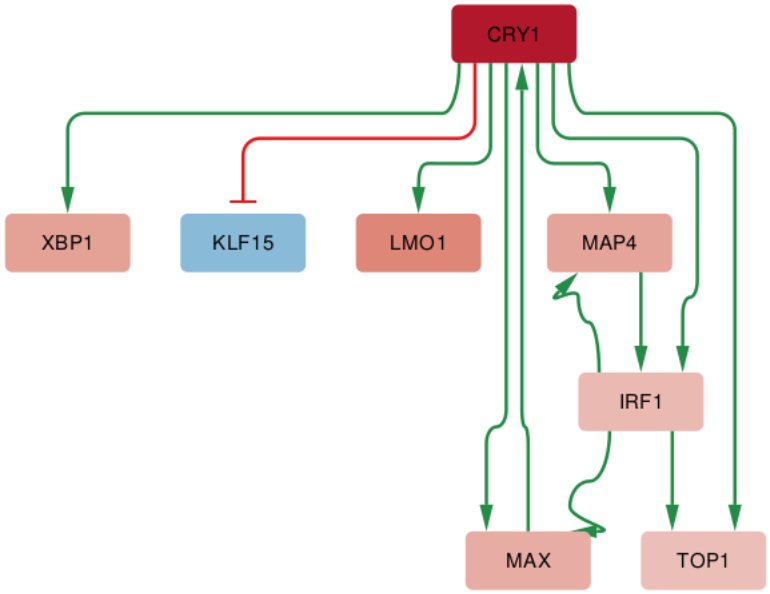

Fig. 5. Treated group network:illustrating how CRY1 activates (green edges) genes as *XBP1*, *LMO1*, *MAP4*, *IRF1*, *MAX*, and *TOP1*, while inhibiting (red edge) *KLF15* . Node color-coding is based on expression changes (see Figure 4 for more information on node coloring).

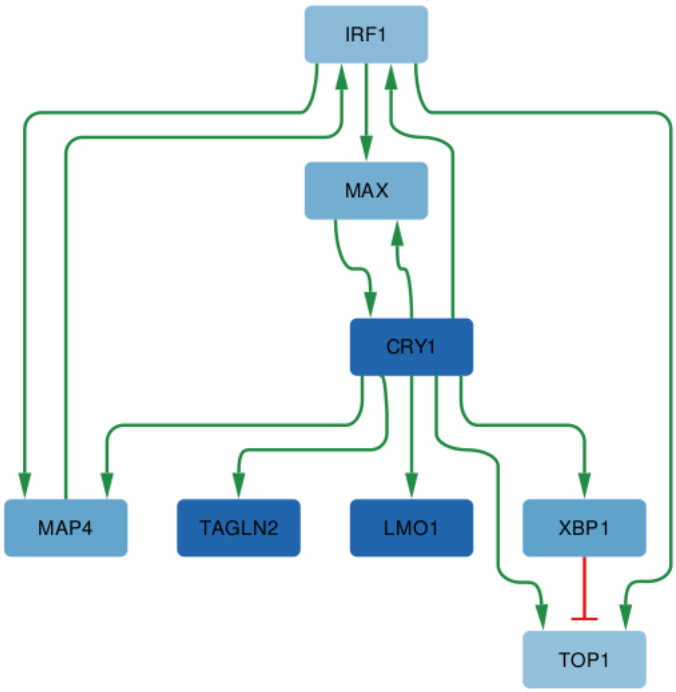

Fig. 6. Control group network: illustrating how *IRF1* and *MAX* regulate *CRY1*, which in turns control downstream genes. Node color-coding based on expression changes (see Figure 4), with red edges indicating inhibitory interactions and green edges indicating activation.

4 DISCUSSION

The objective of this study is to research the relationship between L-DOPA treatment in patients with PD and the development of LID. Our analyses were focused on identifying changes in gene expression and pathways involved in this process. The results of the analyses indicated that cellular stress and inflammation repeatedly appeared as the main topics, suggesting their impact on LID progression.

The gene expression patterns in our analysis match the findings of other studies, showing how L-DOPA treatment affects biological processes in PD patients with LID. One of the main causes of LID is the sensitization of dopamine receptors, especially in the striatum, the part of the brain that controls movement [30]. As L-DOPA increases dopamine levels, these receptors become more sensitive, leading to too much signaling and causing abnormal movements that occur with dyskinesia. Reference [19] states that this receptor hypersensitivity changes the balance of neurotransmitters such as glutamate and GABA, which worsen motor control and, with more time, this makes dyskinesia worse.

LID affects not only movement but also cognitive and mental health. Patients may experience more anxiety, depression, and cognitive decline, partially due to cell stress and neurotransmitter disruptions caused by L-DOPA.

4.1 DGEA findings

In addition to neurotransmitter imbalances, which were discussed in the sources mentioned previously, we found that changes in blood vessels, such as neurovascular remodeling, also play a key role in LID. Studies like [2] show that angiogenesis, which is responsible for the formation of new blood vessels, occurs in the striatum due to L-DOPA treatment. This abnormal overproduction, which was present in our data, linked to the gene *ANGPT2*, might affect how well parts of the brain receive oxygen and nutrients, which can also influence motor symptoms. Genes like *HSPA5*, which help reduce cellular stress, are involved in reducing damage from long-term overactivity of the dopamine receptor. Its upregulation in our data shows that it has been responding to the heightened stress environment [2]. Finally, mitochondrial dysfunction plays a role in this stress response. The gene *LYRM9*, involved in mitochondrial function, is downregulated in LID, suggesting that compromised energy production in neurons also adds to cell vulnerability and cognitive decline [2]. Another factor that affects the progression of LID is synaptic dysfunction in the opioid system. The gene *PDYN*, which controls the production of opioid peptides, is important for movement regulation, which is impacted by this illness. Reference [19] claims that higher levels of dynorphin, resulting from increased *PDYN* activity, disrupt the balance between excitatory and inhibitory signals in the brain, making uncontrollable movements worse. These changes in gene expression help explain the progression of LID and the overall effects of L-DOPA on the brain.

4.2 PEA findings

As for the results of the PEA, we found several pathways that were correlated to inflammation, cellular stress, and metabolic adaptation. The main pathway is related to the processing of proteins in the ER, which includes genes like *HSPA5*, *CALR*, and *XBP1*. They help with the management of misfolded proteins and with the maintenance of cell homeostasis [13]. The upregulation of *HSPA5* in our DGEA aligns with this finding, suggesting that neurons in the striatum activate ER stress pathways to cope with the toxic environment created by L-DOPA [14]. This response could become damaging when maintained over long periods, causing neuronal dysfunction and prolonging dyskinesia, as discussed in Section 4.1 . Another significant pathway is the PI3K-Akt signaling pathway, which supports cell survival and stress response. Genes such as *ANGPT2* and *VEGFA*, previously identified in the DGEA, map to this pathway. Their involvement might highlight the brain's attempt to adapt to the damage caused by L-DOPA through vascular remodeling

and inflammation management [12, 15]. These processes, although protective in the beginning, might also contribute to the abnormal angiogenesis seen in the striatum, making motor symptoms worse. Inflammation and cellular repair processes are also reflected in the enrichment of pathways related to efferocytosis and apoptotic signaling regulation. Efferocytosis, involving genes like *PPARD* and *CALR*, can show the brain's effort to remove damaged cells and manage oxidative stress [13]. It seems that the balance between survival and programmed cell death, as suggested by the control of cell death signals through genes like *XBP1* and *MAP2K6*, is more complex than it appears. In LID, this balance can potentially lead to cell death under chronic stress, which might add to cell loss in the striatum. It is also interesting to note that pathways linked to the circadian rhythm appear to be potentially significant. The enrichment of the circadian regulation pathway, by genes such as *CRY1*, *PTEN* and *KLF9*, suggests a potential link between disruptions in circadian regulation, cellular homeostasis and stress responses. This could make neurons more vulnerable when already under strain from L-DOPA treatment. It is possible that disrupted circadian signals may add to neuroinflammation and metabolic stress, which could lead to dyskinesia. However, it should be noted that the relationship between circadian rhythm disruptions and LID symptoms is correlative, and further studies are needed to establish the cause. While circadian regulation has not previously been linked to LID, these findings highlight the need to research the potential impact of circadian regulation on neuronal health and stress in PD.

4.3 NA findings

The NA shows how gene interactions and regulatory pathways change under L-DOPA treatment. In the treated group (phenotype 1), *CRY1* is the central node, making interactions with genes involved in stress responses, neuronal repair, and structural maintenance, by interacting using activating links with genes such as *XBP1*, *LMO1*, and *MAP4*. The inhibitory interaction between *CRY1* and *KLF15* might shift cell priorities away from metabolic homeostasis to stress management and repair functions which are important for neurodegenerative conditions [8]. This suggests that circadian rhythm genes as *CRY1* may help coordinate cellular adaptation to LID-related cellular stress. The activation of *XBP1*, which is connected to the ER stress pathway, highlights its role in mitigating protein misfolding under neurotoxic conditions [16]. Similarly, the activation of *TOP1*, essential for DNA repair and stability, indicates an effort to possibly address DNA damage caused by both L-DOPA and neuroinflammation [11]. The interactions involving *IRF1* and *MAX* highlight stress response signaling, with targets like *MAP4* which might contribute to cytoskeletal stability [7, 9, 10].

In contrast, the control group (phenotype 2) has a similar network architecture but with differences in expression and interaction strengths. *CRY* remains the main node, as in phenotype 1, but the downstream interactions change. For example, *TAGLN2* is a new gene linked to *CRY1*, likely contributing to stress responses or cytoskeletal remodeling, all of which are processes relevant under L-DOPA-induced stress. This highlights an increased focus on structural integrity in phenotype 2, which could be a way of protecting against the loss of brain cells. *CRY1* shows an activating interaction with *XBP1*, suggesting regulation of stress responses, such as the unfolded protein response [16]. *XBP1*, when activated by stress, inhibits *TOP1's* activity, potentially to regulate DNA repair or transcriptional processes under chronic ER stress [11]. These changes, especially the addition of *TAGLN2* and the regulation of *XBP1*, indicate a different way cells respond to LID. The interactions in the control group focus on maintaining the cytoskeleton, repairing DNA, and controlling transcription, helping to stabilize neuron structure and function. While *CRY1* still affects the circadian and stress-related pathways, the lack of some upregulated interactions seen in the treated group suggests a more balanced response in this group [6]. Together, these findings highlight the interactions between stress responses, circadian regulation, and neuronal homeostasis, giving a new perspective on how neurons adapt to the challenges of L-DOPA treatment.

5 CONCLUSION

This study shows the changes caused by L-DOPA in patients with PD, which result in the manifestation of LID. These gene regulation changes primarily manifest as stress responses, but include neurovascular remodeling and new observations concerning circadian misalignment. Chronic ER stress, shown by the upregulation of *HSPA5* and *XBP1*, might help neurons adapt initially but later leads to dysfunction. Similarly, mitochondrial problems, indicated by the downregulation of *LYRM9*, might worsen energy deficits in already vulnerable neurons. The NA highlights the role of *CRY1*, which interacts with genes such as *TAGLN2* and *MAP4* to maintain cytoskeletal stability. These pathways, while trying to protect cells, sometimes lead to more neuronal dysfunction and worse dyskinesia symptoms with prolonged L-DOPA treatment. Other studies have explored the potential of *HSPA5* drug targets in addressing these issues, with outcomes that can vary depending on the specific cell type or toxin used in the PD model [5]. To ensure appropriate treatment based on findings, more investigation into its neuroprotective properties is necessary. It is not yet clear what effect the circadian rhythm could have on LID in PD patients, so further research in this area could be beneficial. Finally, the comparison of groups reveals clear differences in how neurons respond to L-DOPA-induced stress. In the treated group, the disrupted interactions point to increased cellular stress and an imbalance in repair and metabolism, which may worsen LID. In contrast, the control group shows a more balanced response, with the mechanisms focusing on maintaining structure and controlling gene activity.

6 GLOSSARY

This section contains the Table 3 with all abbreviations used in this document.

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Table 3. Glossary of Abbreviations

Type	Abbreviation	Definition
Gene	ANGPT2	Angiopoietin 2
Gene	CRY1	Cryptochrome Circadian Regulator 1
Gene	HSPA5	Heat Shock Protein Family A (Hsp70) Member 5
Gene	KLF9	Kruppel-Like Factor 9
Gene	KLF15	Kruppel-Like Factor 15
Gene	LMO1	LIM Domain Only 1
Gene	LYRM9	LYR Motif Containing 9
Gene	MAP2K6	Mitogen-Activated Protein Kinase Kinase 6
Gene	MAP4	Microtubule Associated Protein 4
Gene	MAX	Myc Associated Factor X
Gene	PDYN	Prodynorphin
Gene	PPARD	Peroxisome Proliferator-Activated Receptor Delta
Gene	PTEN	Phosphatase and Tensin Homolog
Gene	TAGLN2	Transgelin 2
Gene	TOP1	DNA Topoisomerase 1
Gene	VEGFA	Vascular Endothelial Growth Factor A
Gene	XBP1	X-Box Binding Protein 1
Gene	ZBTB22	Zinc Finger and BTB Domain Containing 22
Gene	PLA1A	Phospholipase A1 Member A
Gene	AMDHD2	Amidohydrolase Domain Containing 2
Gene	CALR	Calreticulin
Gene	ITGA7	Integrin Subunit Alpha 7
Gene	IRF1	Interferon Regulatory Factor 1
Metrics	adj.P.Val	Adjusted P-Value (corrected for FDR)
Metrics	logFC	Log2 Fold Change (expression change between groups)
Metrics	P.Value	Unadjusted P-Value (probability of observed results)
Metrics	t-statistic (t)	Test statistic (evidence against null hypothesis)
Term	DGEA	Differential Gene Expression Analysis
Term	ER	Endoplasmic Reticulum
Term	FDR	False Discovery Rate
Term	GO	Gene Ontology
Term	KEGG	Kyoto Encyclopedia of Genes and Genomes
Term	L-DOPA	Levodopa (L-3,4-dihydroxyphenylalanine)
Term	LID	L-DOPA-Induced Dyskinesia
Term	NA	Network Analysis
Term	PD	Parkinson's Disease
Term	PEA	Pathway Enrichment Analysis
Term	PI3K-Akt	Phosphatidylinositol 3-Kinase-Akt Signaling Pathway
Term	GEO2R	GEO2R Differential Expression Analysis Tool
Term	DEG	Differentially Expressed Gene

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