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A Study To Explore How Faulty Gene Expressions Cause Diseases. A Suitable Early Detection And Treatment May Permanently Cure Many Types Of Inherited Diseases

DAI YongXia[1], Nurul Azmir Bin Amir Hashim[2], Suriyakala[3]

[1] daiyongxia_1982@163.com

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Abstract
A disease's aetiology is often complex, including both hereditary and environmental influences. Medical (by facilitating medication development and tailored treatment) and scientific (by illuminating the mechanical and evolutionary components of disease) goals are served by the discovery of major genetic components. A number of genetic approaches have established associations between diseases and specific regions of the genome. These include association studies and linkage analysis, which map the correlation between alleles at distinct loci and unite sites that tend to be inherited together. Studies of this kind look at hundreds of genes, which is much too many to test experimentally for possible disease codes. It follows that computational approaches for determining whether or not certain genes within a given chromosomal region may encode disease genes are very beneficial. There is a significant amount of evidence showing that many illnesses are susceptible. variances in the rates of gene expression among different kinds of cells. In particular, a gene's involvement in disease is likely to be supported by the fact that it is more prevalent in sick individuals compared to healthy ones. To identify the variations in expression levels, microarray experiments were the most common.

KEYWORDS: *Gene Expression, Hereditary Diseases, Genetic, Disease.*

1. INTRODUCTION

When most people consider genetic illnesses, they usually think of uncommon, single-gene disorders as cystic fibrosis (CF), phenylketonuria, or haemophilia. Though there are hundreds of uncommon illnesses, genetic problems account for 80%. Because of their frequency, about one in 17 people have an odd ailment. Furthermore, depending on each individual, their great DNA variations influence all disease processes, even common ones to different degrees. One or more of these factors may increase a person's sensitivity to one ailment—say, cancer—while the same person may be less sensitive to another—like diabetes. Though their biochemical and physical reactions may vary depending on heredity, environmental factors such nutrition and exercise in diabetes influence many illnesses. Their responses to illnesses depend on their genes, hence the population is quite varied. Most cancers arise from a lifetime of environmental or maybe hereditary genetic alterations. Understanding disease processes and developing successful treatments, prevention, and interventions depends on knowledge of genes and the whole genome as well as their variations in the human population (Alhusani, 2019).

Gene-environment interactions define many illnesses. Identification of important genetic variables supports scientific (mechanistic and evolutionary illness features) as well as medical (medication development and tailored treatment) goals. Linkage analysis and association studies are two examples of genetic techniques that have shown many relationships between diseases and certain chromosomal regions. Usually spanning hundreds of genes on chromosomal areas, too many for reasonable experimental investigation of disease genes. Therefore, computer approaches help to estimate the likelihood of disease genes in a chromosomal region. One is aware of predisposition to some illnesses. variations in individual cells' gene expression (Cotta, 2020). For example, a

cluster of genes is probably related to disease if it is more common in sick people than healthy persons. Expression levels were found via microarray tests. Certain studies have shown that genes linked to the same disease generate interacting protein products. A further characteristic of a disease gene is that its protein output is strongly linked with other genes producing diseases. Few computer techniques have used this to identify genes causing diseases in interactions between proteins. Recent attempts to combine many contributions have revealed nearby disease-causing genes as well as differential expression genes for disease. This group comprises techniques based on hypotheses about geographically close disease gene protein products in the protein interaction network. Only approximation, greedy methods can examine large protein networks as genes express at various levels (Lieto, 2019).

2. BACKGROUND OF THE STUDY

Transcriptional control is key to gene expression. Functional and evolutionary genomic architecture investigations are only beginning to reveal its intricate regulation system. Multiple regulatory components, including the promoter, ensure gene expression at the optimum time and quantity. Introns above and downstream of the transcription unit may include enhancers and repressors (Greene, 2017). Critical developmental control genes have complicated expression patterns therefore their cis-regulatory domain may extend beyond the transcription unit. Early insights came from disease-related chromosomal breakage in unrelated genomic domains. Large-scale genome sequence comparisons show numerous conserved noncoding regions. Recent functional evaluations show that many conserved regions are transcriptional regulatory elements present in distantly related neighbouring genes. DNA-binding protein binding sites that are only expressed in certain organs are often conserved. Chromatin conformation changes during development may impact protein accessibility and transcriptional regulation (Kleinjan, 2016). These delicate systems may fail and cause illness. Regulatory element mutations cause distinct symptoms than coding region mutations. Researchers and clinicians benefit from maternally transmitted genetic illness mothers and siblings. Mothers who pass on hereditary illnesses to their children may feel humiliated, unhappy, and self-blame. Guilt from continual accusing may harm moms' mental health and the marriage. Few research has examined impaired children's siblings' positive and negative responses by heredity. A sibling who learns their brother has LHON may worry about going through it. Research showed that spirituality and perceived social support were the biggest buffers for challenged families. Parents and siblings of handicapped people use these features to varying degrees while dealing with hereditary diseases. Mothers and siblings of Leber's hereditary optic neuropathy patients were evaluated for risk factors (Konig, 2017). Diseases influence energy-generating mitochondria. Multiple mitochondrial diseases may result from faulty mitochondrial DNA. Diabetes, visual neuropathy, and muscular disorders are examples. Mitochondrial DNA gene changes increase this disease risk. Mutations should have different effects as mitochondria exist in all cells except erythrocytes. Genetic point mutations affect one DNA nucleotide. Due to scientific and technological advances, mitochondrial DNA may now be used to detect the LHON gene (Simeoni, 2016). One-nucleotide DNA alterations are genetic point mutations. Mutations may occur spontaneously or via exposure. In 95% of instances, A causes LHON. Although some genes produce similar symptoms, they differ. Although the most prevalent gene, the 11778 gene has the lowest spontaneous sight return rate at 4%. Vision recovery is 70% for the 14484 gene and 40% for the 3460 gene.

3. THE PURPOSE OF THE RESEARCH

The results of this research will show that transcriptional regulation is one of the most important methods for controlling gene expression. The complex machinery required to carry out this control is only now being partially understood via functional and evolutionary studies of genomic architecture. To maintain consistent, time-and amount-appropriate gene expression, the promoter is only one of several regulatory components required. It is possible to find enhancer and repressor elements in introns and upstream and downstream of the transcription unit, respectively. Critical developmental control genes and other genes with complex expression patterns may have a cis-regulatory domain that extends much beyond the transcription unit. One of the first signs of this was chromosomal breaks linked with diseases that were located distant from the gene in question. Thanks to the ability to now compare genomes across different species, researchers have found that a lot of noncoding regions are very conserved. Functional studies have shown that many of these conserved sites are transcription regulatory elements; these sites may be located in genes that at first glance seem to have no relationship to one another. Some of these conserved sequences have DNA-binding protein binding sites that are expressed in certain organs. Changes in chromatin conformation throughout development may regulate transcription and regulate protein access to these sites. Misalignment of these intricately regulated systems may lead to disease. Individuals with

coding-region modifications will not experience certain symptoms associated with changes in regulatory components (Pilling, 2019).

4. LITERATURE REVIEW

They used microarray global gene expression data and a human genome-sized protein-protein interaction network to prioritise disease-related genes. Their Katz centrality score was based on the fact that illness genes cluster near one other in the protein network. Scores may be achieved using two-factor calibration (Lu, 2020). These variables' ideal values may provide biologically significant responses. The first parameter, w, determines the protein interaction network's expression level and proximity priorities. The second parameter, g, estimates the chance that a non-differentially expressed node is a disease gene (Schrier, 2019). This suggests that the protein-interaction network and differential expression might be used to prioritise illness genes. However, the interaction provides more information than microarray data to predict undiscovered disease genes in their condition. By using inadequate data on known disease genes, they enhanced their technique. When scientists rated all genes globally instead of concentrating on individual gene loci, they uncovered genes with high pleiotropy that are involved in many illnesses' physiological pathogenic processes. The network discovery of genes linked in several illnesses supports the phenotypic dependency, cooccurrence, and common pathogenesis of these conditions. A unique, user-friendly technique for rating potential disease genes is presented in this work. This method may also compare genetically similar diseased symptoms (Simeoni, 2016).

They hypothesised that literature and microarray data would differ at the start of their investigation. Although microarray data are resistant to publication bias, the literature is clearly influenced by earlier studies. They wanted to quantify this bias by comparing their findings to microarray "ground reality". They were mistaken in believing literature and microarray data were always linked, but this was not the case. The FC threshold may not correlate with biological activity for all genes. Additionally, an expression study's findings may differ based on the FC threshold. They observed that high FC requirements lead to publications using microarray expression data that may not adequately represent biological processes (Esteban, 2017).

- **The Diversity of Human Genetic Variation.**

Genetic variation arises from stochastic errors that occur during the process of DNA replication. It is important to note that these mutations are only inherited by offspring when they affect germ line cells.

Genetic variation can be categorised into two main types based on its magnitude: point mutations and structural variants. Single nucleotide polymorphisms (SNPs) are the predominant form of variation in the human genome (Chien, 2019). They are characterised by single base pair differences. On the other hand, structural variants encompass a heterogeneous class of genetic variations. These variants range from small insertions, deletions, and inversions of a few base pairs to large structural changes that span several megabases and involve chromosomal rearrangements. In addition to mutations, recombination serves as an additional mechanism for generating variation within our genome. Mutations are responsible for generating new variations, whereas recombination is the process during meiosis where homologous chromosomes from both parents align and exchange consecutive sequences, resulting in the rearrangement of existing variants within the same chromosome (Yang, 2016).

The release of the initial human genome sequence in 2001 signified a significant milestone in scientific history and likely had a profound impact on molecular biological research in the present century. The event not only served as a significant scientific milestone, but also laid the foundation for a paradigm shift in the field of biology, establishing the fundamental principles that underpin various "-omics" disciplines (Balwani, 2020).

5. RESEARCH QUESTION

i. What are the diseases that can be detected through genetic testing?

6. RESEARCH METHODOLOGY

To investigate the research topics and test the hypotheses, this study used causal comparative and correlational methods. The former was used to compare LHON-affected individuals to the normative population, while the latter was used to identify associations between variables. The poll was conducted using SurveyMonkey, a free online survey platform.

Sampling: The subjects in this study were 117 patients sampled from the total population of the Gene Expression.

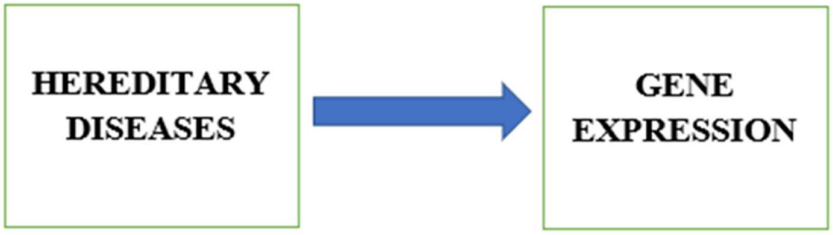
Data and Measurement: The data were collected during the first half of the annual year 2022. Gene expressions were required. Questionnaire was distributed and quantitative analysis was implemented.

Statistical Software: MS-Excel and SPSS 25 Was used for Statistical analysis. The SurveyMonkey data file was

imported into SPSS 25.0 (Statistical Package for the Social Sciences). The data was transferred and validated in accordance with industry standards before any formal statistical analysis was performed. To produce statistics on outlying data points, probable outliers, and missing data, SPSS's Explore tool was used. To further investigate the distribution of major research variables and their suitability for parametric, we created histograms and measurements of skew and kurtosis using the Frequency function in the SPSS analytic software.

Statistical Tools: Descriptive analysis Was applied to understand the basic nature of the data. Validity and reliability of the data Was tested through Cronbach alpha, and T test.

I) CONCEPTUAL FRAMEWORK



7. RESULTS

- **Reliability**

Cronbach's alpha values calculated from the research sample show that all of the measures are trustworthy (Table 1). One way to evaluate reliability is via Cronbach's alpha. Cronbach's alphas for all of the study's metrics were more than.76. Therefore, you can rely on them. Theoretical Findings I. Research The primary research question was: How do moms of children with Leber's hereditary optic neuropathy feel about their own mental health? The study's premise was that compared to a normative sample, women whose children had Leber's hereditary optic neuropathy (LHON) symptomatology would have considerably greater levels of psychological distress, interpersonal issues, and social role failure. This hypothesis was examined using a battery of independent t tests based on a single data set.

Table1: Cronbach's alpha (Reliability)for all scales

Scale	# of items	Cronbach`s Alpha
SIBS total	27	.78
IES Total Score	15	.89
IES Intrusive	7	.90
IES Avoidance	8	.80
MSPSS Total Score	12	.91
MSPSS Significant Other	4	.92
MSPSS Family	4	.91
MSPSS Friends	4	.90
OQ-45 Total Score	45	.95
OQ-45-Symptom Distress	25	.92
OQ-45-Interpersonal Relations	11	.86
OQ-45-Social Role	9	.76

Mothers' mean OQ-45 Total scores were 48.65 (SD = 24.40), above the normative sample mean of 45.00. A one-sample t test compared the average mother's OQ-45 Total score to the normative sample mean (Table 2). The mother's score was similar to the normative 45 (t(59) = 1.15, p =.251).Moms scored 10.80 (SD = 6.98) on the OQ-45 Interpersonal Relations measure, compared to 10.00 for the normative group. A one-sample t test comparing mothers' mean OQ-45 Interpersonal Relations scores to a normative sample is shown in Table 2. Moms' average score was not statistically different from the normative mean score of 10.00 (t(59) = 0.88, p =.378).

Mothers' mean OQ-45 Social Role scores were 8.68 (SD = 5.03), below the normative sample mean of 10.00.

Mothers' mean OQ-45 Social Role subtest scores were compared to the normative sample mean using a one-sample t test (Table 2). Compared to the normative mean score, the mothers' mean score was significantly lower (t(59) = -2.02, p =.047). Mothers scored far worse on Social Role tests than the normative group. Mothers scored 29.16 (SD = 14.47) on the OQ-45 Symptoms Distress scale, compared to 25.00 for the normative population. A one-sample t test compared the average mother's OQ-45 Symptoms Distress score to the normative sample mean of 25.00 in Table 2. Compared to the normative mean score, the mothers' mean score was significantly different (t(59) = 2.22, p =.030).

The average Symptoms of Distress score for moms was well above the norm.

Table 2: One sample T Test for Mothers' OQ45 Total Scores and Subscales

	N	Mean	*SD*	Mean difference	*t*	*df*	*P*
OQ Total Score	60	48.65	24.40	0.80	1.15	59	.251
OQ Interpersonal Relations	60	10.80	6.98	0.80	0.88	59	.378
OQ Social Role	60	8.68	5.03	-1.31	-2.02	59	.047*
OQ Symptoms Distress	60	29.16	14.47	4.16	2.22	59	.030*

*$p<.05$

Researchers discovered some evidence that moms of children with Leber's hereditary optic neuropathy (LHON) had greater levels of psychological distress, interpersonal issues, and social role dysfunction than a normative group. In instance, moms scored lower on the Social Role (M = 8.68) than a normative group (M = 10.00). Mothers had a higher average Symptom distress score (M = 29.16) than a normative group (M = 25.00), suggesting greater psychological suffering.

First hypothesis conclusion. This research asked: How do mothers of children with Leber's hereditary optic neuropathy feel about their mental health? The research hypothesised that mothers whose children had Leber's hereditary optic neuropathy (LHON)-related vision loss would have more psychological distress, interpersonal difficulties, and social role dysfunction than a normative group. The investigation only partially supported the researcher's hypothesis. Mom's average Social Role score was 8.68, far lower than the normative sample's 10.00. This contradicts the idea

that moms have more social role disorder. Moms exhibited far higher psychological suffering than a normative group (M = 29.16 on the Symptom suffering scale vs. M = 25.00). Results for Hypotheses 3 and 4.How can spirituality affect LHON-related vision loss mothers' emotional health? Researchers predicted a favourable correlation between religiosity and moms of children with LHON-associated visual impairments. The mothers of LHON-related vision loss: Does social support affect emotional well-being? The research hypothesised that mothers of children with LHON-related visual impairment would report a positive link between social support and mental wellbeing. For this, various regression models were created. Regression model results are summarised below. The IES and its subscales were dependent variables in one regression analysis. The OQ-45 and subscales were dependent variables in the second regression model.

Assessing LHON maternal IES risk. As the dependent variable in the initial regression models, IES and subscales were created. MSPSS Total Score, SIBS, and total IES scores (the dependent variable) were evaluated in a first regression model. The independent variables and model were updated simultaneously. The model did not reach statistical significance (F(2, 65) =.365, p =.69) and described just 1% of IES score variance (R2 =.01). Table 3 shows regression coefficients. IES scores were unrelated to independent variables. Since the regression model was insignificant, the coefficients were ignored.

The MSPSS subscales, SIBS, and the IES Avoidant Subscale (the dependent variable) were the focus of the subsequent regression model. At the same time, we fed in all of the independent variables. Overall, the model's lack of significance was shown by its inability to explain more than 7.6% (R2 =.076) of the variation in the IES Avoidant Subscale (F(4, 53) = 1.090, p =.371). Table 4 displays the regression coefficients. There was no statistically significant relationship found between any of the independent factors and IES Avoidant Subscale scores. Since the total regression model was not significant, the coefficients of the regression were not analyses.

Table 3: Regression Coefficients for the Model Examining the Relationship between the MSPSS Total Score, the SIBS and the Overall IES Score

Model	*B*	Std. Error	*β*	*t*	*p*
SIBS Total score	-.016	.125	-.019	-.129	.898
MSPSS Significant Other	-.155	.363	-.083	-.427	.671
MSPSS Family	-.420	.355	-.239	-1.186	.241
MSPSS Friend	.275	.369	.116	.745	.460

Table 4: Regression Coefficients for the Model Examining the Relationship between the MSPSS Total Score, the SIBS and the Overall IES Score

Model	*B*	Std. Error	*β*	*t*	*p*
SIBS Total score	.060	.099	.089	.060	.544
MSPSS Significant Other	.399	.285	.270	1.398	.168
MSPSS Family	-.396	.279	-.284	-1.418	.162
MSPSS Friend	.251	.290	.134	.863	.392

Predicting the OQ-45 in LHON moms.The following collection of regression models used OQ-45 and its component scales. The correlation between MSPSS total score, SIBS, and OQ-45 total scores (dependent variable) was investigated in the first regression model. At the same time, we fed in all of the independent variables. The whole model was statistically significant ($F(2, 55) = 9.61$, $p = .00$), and it explained 25% ($R2 = .25$) of the variation in the OQ-45.

8. DISCUSSION

This research examined the mental health of mothers and siblings of Leber's Hereditary Optic Neuropathy patients. The research also evaluated whether perceived social support and spiritual participation and beliefs protect these family members when their kid or sibling becomes disabled. Compare the new study's conclusions to previous studies. This report will also discuss the study's shortcomings, clinical implications, and future research.

This investigation supported the fourth theory. Siblings had more psychological suffering than a normal population. The average OQ-45 Total score of siblings was considerably higher than the normative group, suggesting increased distress. The average Symptom suffering score of siblings was considerably higher than that of the normative group, indicating more symptom-related suffering. The research indicated that siblings had more interpersonal issues and social role dysfunction than a normative group. This theory suggests that siblings of LHON patients with visual loss symptoms encounter severe difficulty in seeing their sibling develop a handicap. Unlike moms of visually impaired children, the primary hypothesis of this research was that LHON patients had considerably higher degrees of symptom discomfort, interpersonal problems, and social dysfunction. Although moms may have a specific trait or conduct, they must assist and care for their disabled siblings. Leber's hereditary optic neuropathy (LHON) carriers may lose their eyesight at any age, like their siblings. Apprehension and uneasiness about this situation explain siblings' increased psychological suffering. Interpersonal issues may occur. The family member without the hereditary issue has these symptoms due to emotional events that cause them to withdraw, isolate, or act out. An additional idea is that many people with Leber's hereditary optic neuropathy (LHON) are young adults who behave like their age group. LHON mutation carriers should avoid drinking and smoking to reduce visual loss risk.

9. CONCLUSION

This article shows how Next-generation DNA sequencing may be used to find variants linked to diseases and understand their genetic structure. The current state of the art allows for the efficient examination of a large

number of genetic variations in a single, cost-effective experiment.

In addition, there is a great chance to show how genes with variations that cause genetic illnesses behave in the many current biological datasets. It has The widespread collection of genetic data raises many moral, legal, and societal questions, yet in the near future, medical practice will likely shift towards sequencing and data analysis powered by IT. It is believed that this change would lead to a plethora of small-scale discoveries that, when aggregated, will provide the way for customised treatment. Since DNA was discovered to be the bearer of our genetic information, our knowledge of the human genome has progressed considerably. Despite the immense amount of data produced by sequencing the human genome, there are still many obstacles to overcome before this information can be understood and explained. Capable of drawing on current data to provide new insights.

We spoke about a computational analysis pipeline and a web app that can combine genetic data with phenotypic data and analytical results. In contrast to the importance of protein structure, this method takes into account the potential that the exact sequence of nucleotides may not be as crucial for maintaining proper gene expression via non-coding regions. Therefore, it may be useful to use models that give more weight to different parts of non-coding DNA sequences when investigating their link to diseases. This includes things like the amount of copy number variations that could affect the three-dimensional structure of DNA. As a solid groundwork for future methodological advances in this area, the study offered in this thesis will be useful for investigating the variability that affects the genome's regulatory regions.

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