Common Characteristics of Alzheimer's Disease and Parkinson's Disease Based on AlzGene and PDGene Databases

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INTRODUCTION

Alzheimer's disease (AD) and Parkinson's diseases (PD) are two of the most common neurodegenerative disorders, characterized by loss of substantial neurons. Many previous studies have provided insights into the impacts of genetic factors on AD and PD, and some common clinical, pathological, and genetic characteristics have also been dissected. But the explicit correlation between the two diseases have yet to be elucidated. In this study, we first extracted significantly associated genes from both two databases, namely, AlzGene and PDGene. Then we analyzed the biological function of the two gene sets by The database for annotation, visualization, and integrated discovery (DAVID) and Ingenuity Pathway Analysis (IPA), respectively. Lastly, we identified the common parts of the enriched GO biological process terms and pathways in the two disease-specific gene sets. Our work identified lipid metabolism as one of the common parts between AD and PD, consistent with previous study. Our results show that there are many overlapping relevant cellular components and biological functions between AD and PD and these common parts of the two diseases were potential targets for further analysis and replication study.

MATERIALS AND METHODS

Identifying common characteristics of AD and PD based on AlzGene and PDGene databases

From the AlzGene and PDGene databases, genes showing significant association with AD and PD were extracted, respectively. Then, the two gene sets were analyzed using the bioinformatics resource DAVID and IPA, and the enrichment of given pathways and Gene ontology (GO) terms in the overlapping gene list was measured by Fisher exact test p-value, and FDR, a multiple comparison p-value correction based on the method of Benjamini and Hochberg. In the end, we identified the common parts of AD and PD in terms of GO biological process term and pathway. The framework of our study was shown in Figure 1.

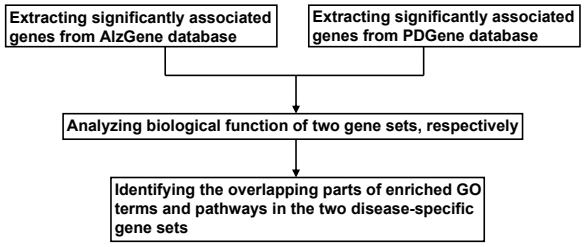

Figure 1. The flow chart for identifying common characteristics of AD and PD based on AlzGene and PDGene databases

Data collection from PDGene and AlzGene databases

AlzGene (http://www.alzgene.org) and PDGene (http://www.pdgene.org) are databases including many genetic studies about AD and PD, separately. And we extracted genes with one or more "Positive", a criterion of these two databases indicating significant (P<0.05) association with PD or/and AD.

Biological function analysis of the two disease-specific gene sets

The specific relation of the two related gene sets with AD and PD was evaluated by analyzing the GO biological processes or biochemical pathways enriched in these genes. The biological functions were analyzed by The database for annotation, visualization, and integrated discovery (DAVID) and Ingenuity Pathway Analysis (IPA).

DAVID was used for GO term enrichment analysis. To simplify the analysis, only GO biological processes terms were selected. The exported GO terms were filtered by false discovery rate (FDR), only those with FDR value smaller than 0.05 were kept and top 10 terms were extracted.

Biochemical pathways enriched in the two disease-specific genes were analyzed by IPA, separately, with the goal of revealing the enriched biochemical pathways. All the pathways with one or more genes overlapping the candidate genes were extracted. The exported pathways were filtered by false discovery rate (FDR), only those with FDR value equal to or smaller than 0.01 were kept.

RESULTS

A) Identification of genes in PDGene and AlzGene reported to be significantly associated with AD and PD

There were 213 and 357 significantly associated genes extracted from PDGene and AlzGene, respectively. After excluding vague loci, pseudogenes and predicted genes, 211 and 350 genes were retrieved for PD and AD, separately.

B) Enriched Gene Ontology (GO) terms (biological processes) based on genes associated with AD and PD

The top 10 enriched GO biological processes of PD- and AD-related genes are retrieved, and the common parts of AD- and PD-associated GO terms include response to chemical stimulus and response to stress. This outcome was consistent with the conclusion of previous work.

C) Enriched biological pathways associated with AD and PD

The top 10 enriched pathways of PD- and AD-related genes are shown in Figure 2. And we identified 6 overlapping pathways between the two diseases. As one of the top significant pathways, LXR/RXR activation is shown in Figure 3, and the common and unique parts of this pathway are represented in different colors.

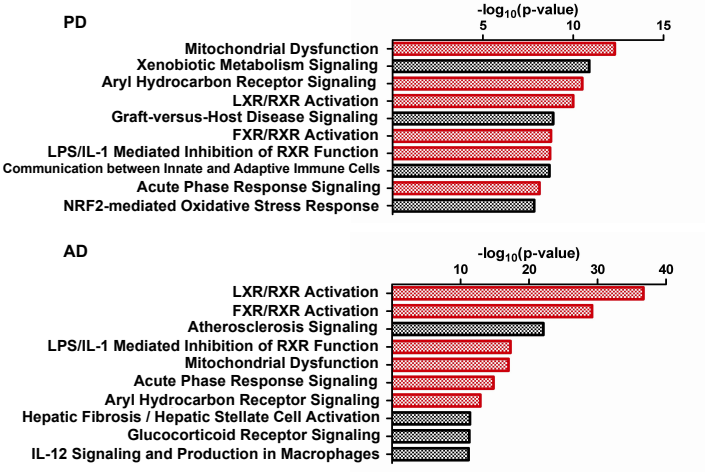

Figure 2. Top 10 pathways significantly enriched in AD- and PD-related genes and the overlapping parts are shown in red.

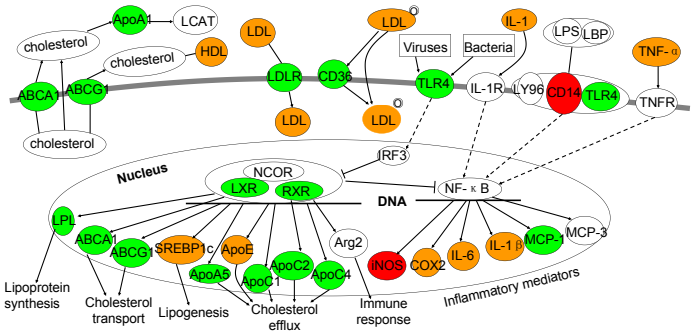

Figure 3. Schematic representation of LXR/RXR activation in macrophage, and corresponding genes related to AD and PD are shown together. The PD-specific and AD-specific genes, as well as the overlapped genes, are shown in red, green and yellow, respectively.

SUMMARY

1. In this study, we collected significantly associated genes from AlzGene and PDGene, respectively. And then we evaluated the biological function of the two gene sets, and discovered four main biologically functional classification, i.e., stress-associated pathways, lipid metabolism-associated pathways, immune response-related pathways and mitochondrial dysfunction-associated pathways. These findings were consistent with previous study.
2. Although there are some common pathways in both AD and PD, the mechanisms underlying these overrepresented pathways are distinct.