Original Article

Physiological genomics analysis for Alzheimer's disease

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Abstract

Alzheimer's disease is a common kind of dementia. This disorder can be detected in all countries around the world. This neurological disorder affects millions of population and becomes an important concern in modern neurology. There are many researches on the pathogenesis of Alzheimer's disease. Although it has been determined for a long time, there is no clear-cut that this is a case with genetic disorder or not. A physiological genomics is a new application that is useful for track function to genes within the human genome and can be applied for answering the problem of underlying pathobiology of complex diseases. The physiogenomics can be helpful for study of systemic approach on the pathophysiology, and genomics might provide useful information to better understand the pathogenesis of Alzheimer's disease. The present advent in genomics technique makes it possible to trace for the underlying genomics of disease. In this work, physiological genomics analysis for Alzheimer's disease was performed. The standard published technique is used for assessment. According to this work, there are 20 identified physiogenomics relationship on several chromosomes. Considering the results, the HADH2 gene on chromosome X, APBA1 gene on chromosome 9, AGER gene on chromosome 6, GSK3B gene on chromosome 3, CDKHR1 gene on chromosome 17, APPBP1 gene on chromosome 16, APBA2 gene on chromosome 15, GAL gene on chromosome 11, and APLP2 gene on chromosome 11 have the highest physiogenomics score (9.26) while the CASP3 gene on chromosome 4 and the SNCA gene on chromosome 4 have the lowest physiogenomics score (7.44). The results from this study confirm that Alzheimer's disease has a polygenomic origin.

Key Words

Alzheimer's disease, physiogenomics, relationship

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Ann Indian Acad Neurol 2013;16:72-4

Introduction

After success in the Human Genome Project, bioinformatics is widely used in medicine, and genomics is widely used in medical research.[1] Of several applied genomics, physiological genomics is a new application that is useful for track function to genes within the human genome. Basically, the genome can relate to physiology.[1] The physiogenomics can be helpful for study of many complex diseases. Alzheimer's disease is the most common kind of dementia in the US and around the world with exponential increasing rates in the elderly aged above 65.[2] Increases in life expectancy in the present day results in a large number of people living to old ages and will result in a quadrupling of Alzheimer's disease cases in the past few years.[2]

Although Alzheimer's disease has been known for a long time, it is still doubtful whether this is genetic disorder or not.[3] Several reports noted for a significantly different distribution, in patients and controls, of proinflammatory genes, alleles of which are usually under-represented in controls and excessively represented in patients affected by Alzheimer's disease.[4] Systemic approach on the pathophysiology and genomics might provide useful information and help the medical scientist better understand the pathogenesis of Alzheimer's disease. In this work, physiological genomics analysis for Alzheimer's disease was performed. The purpose of this work is to assess which genes have physiogenomic correlation, which further implies relation to ethiopathogenesis, to Alzheimer's disease.

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.107711

Materials and Methods

This work is a simulation-based study using bioinformatics concept. The physiogenomics analysis by consomics technique[5,6] is presently used for development of many physiogenomics tools including PhysGen, which was used for all simulations in this study. Briefly, this tool is for testing functionality of relevant genes using a novel strategy, TILLING (Targeting Induced Local Lesions in Genomes) assay, which provides a standard reverse-genetic strategy helping detect allelic series of induced point mutations in genes of interest. [7,8] In this work, the assigned primary template was the human genome. The input ontology term is "Alzheimer's disease." Gene in range v 2.02 with length 1 Mbp was focused in the

analysis. The resulted identified gene accompanied with its specific physiogenomics score, which implies degree of correlation (it is considered significant high or correlate if score is more than 1, and a higher score means higher relationship), is derived. All protocols in this work are the same as previously used in the previous serial international publications by Wiwanitkit.[9,10]

Result

There are 20 identified physiogenomics relationship on several chromosomes as demonstrated in Table 1. Different of physiogenomic score can be seen [Table 1]. According to this work, the *Hydroxyacyl-Coenzyme A* dehydrogenase, type 2 (HADH2) gene on chromosome X, Amyloid beta A4 precursor protein-binding family A member 1 (APBA1) gene on chromosome 9, advanced glycosylation end product-specific receptor (AGER) gene on chromosome 6, *Glycogen synthase kinase 3 beta* (GSK3B) gene on chromosome 3, Cyclin-dependent kinase homologous recombination 1 CDKHR1 gene on chromosome 17, Amyloid beta precursor protein-binding protein 1 (APPBP1) gene on chromosome 16, Amyloid beta A4 precursor protein-binding family A member 2 (APBA2) gene on chromosome 15, Galactose (GAL) gene on chromosome 11, and Amyloid beta (A4) precursor-like protein 2 (APLP2) gene on chromosome 11 have the highest physiogenomics score (9.26) while the Caspase 3 (CASP3) gene on chromosome 4 and the Alpha-synuclin (SNCA) gene on chromosome 4 have the lowest physiogenomics score (7.44).

Table 1: Physiogenome for Alzheimer's disease

Genes	Chromosome	Physiogenomic score
HADH2	X	9.26
APBA1	9	9.26
VLDLR	9	9.06
ABCA1	9	7.87
CTSB	8	9.06
AGER	6	9.26
CASP3	4	7.44
SNCA	4	7.44
GSK3B	3	9.26
TGFB1	19	8.59
CDKHR1	17	9.26
MAPT	17	7.87
APPBP1	16	9.26
APBA2	15	9.26
PSEN1	14	9.16
PSEN2	1	8.96
IDE	10	9.16
GAL	11	9.26
APLP2	11	9.26
A2M	12	8.96

Discussion

Alzheimer's disease is an important disorder in geriatric neurology. Behavioral and functional change is the important classical clinical manifestation, and this specific disorder requires properly management.[11] Exact etiopathogenesis of Alzheimer's disease is very complicated and still partially unknown. Its etiology might be possibly determined by the interaction of genetic and environmental factors.[12] Alzheimer's disease genetics may be one of the most widely published areas in neurological science.[13] Three early-onset Alzheimer's disease genes with causative mutations (APP, PSEN1, PSEN2) and one late-onset Alzheimer's disease susceptibility gene, apolipoprotein E (APOE) are widely mentioned.[13] The genetic contribution seems to be important, but this might be a polygenic type.[12] It is still a question whether hereditary Alzheimer's disease in humans is existed or not. Analysis of gene expression in Alzheimer's disease is a present direction of Alzheimer's disease research.

Here, the author used the physiogenomis approach to study the physiogenome in Alzheimer's disease. According to this work, the simulation shows that there are 20 genes that have genetically relationship to the ethiopathogenesis of Alzheimer's disease. The identified genes had difference in its phylogenomics property. The genes with high physiogenomics correlation implies their strongly correlation to the physiological phenotype. Of 20 identified genes, 9 genes have the highest physiogenomics score meaning that these genes have strong physiogenomic correlation to Alzheimer's disease. The results from this study are concordant with a recent metabolomic study.[14]

Concerning HADH2 gene on chromosome X, HADH2 is proved to be an enzyme involved in the mitochondrial dysfunction detectable in the Alzheimer's disease.[15] Concerning APBA1 gene on chromosome 9, it is reported as a third member of the X11 protein family interacting with Alzheimer's beta-amyloid precursor protein.[16] Concerning AGER gene on chromosome 6, there is no direct report, but there is a report indicating that the load of *Chlamydia pneumoniae* in the Alzheimer's brain varied with APOE genotype.[17] Concerning GSK3B gene on chromosome 3, there is also no direct report, but it is mentioned in the cerebral cholesterol shuttle in cases of Alzheimer's disease.[18] Concerning CDKHR1 gene on chromosome 17, there is also no direct report. Concerning APPBP1 gene on chromosome 16, there is also no direct report. Concerning APBA2 gene on chromosome 15, it encodes phosphotyrosine-binding domain proteins that interact with the Alzheimer's disease amyloid precursor protein.[19] Concerning GAL gene on chromosome 11, there is also no direct report. Concerning APLP2 gene, APLP2 mRNAs had previously been quantified in Alzheimer's disease *specimen*.[20] The results from this study confirm that Alzheimer's disease has a polygenomic origin.

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How to cite this article: Wiwanitkit V. Physiological genomics analysis for Alzheimer's disease. Ann Indian Acad Neurol 2013;16:72-4.
Received: 27-05-11, **Revised:** 26-01-12, **Accepted:** 21-06-12
Source of Support: Nil, **Conflict of Interest:** Nil