

Profiling Alzheimer Gene Relationships Using Bayesian Networks

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Alzheimer's disease (AD), a progressive neurodegenerative disease characterized by plaque buildup in the brain, is one of the leading causes of death in older Americans. Many risk factor genes have been proposed, but relationships among them are not well understood. In this study, we focus on the genetic risk factors Apolipoprotein E (APOE), Amyloid Precursor Protein (APP), and Presenilin 1 and 2 (PSEN1 and PSEN2). APOE has been considered the greatest genetic risk factor for AD. It is believed that the characteristic amyloid beta plaques in the AD brain are a result of the cleaving of APP by γ -secretase, which is encoded by PSEN1 and PSEN2. Older adults and females have an increased risk for AD. The hippocampus is the most severely affected brain region in AD, so we focused on the gene expression profile of the hippocampus compared to other brain regions. This project aims to use Bayesian Networks to model the relationships and patterns of major genetic and clinical AD risk factors with brain microarray datasets available on the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) database. A Bayesian Network model incorporating background knowledge of AD risk factor relationships was compared to a model derived from our data. The background knowledge model scored just as well or better than the model derived from our data. These models indicated that increased expression of APOE and decreased expression of APP, PSEN1, and PSEN2 are linked with increased AD risk. Female and hippocampal samples tend to have greater dysregulated gene expressions compared to males and non-hippocampal regions. Further analysis on these models and relationships is required, but elucidating the patterns of the risk factors highlighted here allow future research to build and include other clinical and genomic risk factors that may improve understanding and treatment of AD.