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Analyzing the genes related to Alzheimer's disease via a nework and pathway-based approach

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Motivation and Aim: Our understanding of the molecular mechanisms underlying Alzheimer's disease (AD) remains incomplete. Previous studies have revealed that genetic factors provide a significant contribution to the pathogenesis and development of AD. In the past years, numerous genes implicated in this disease have been identified via genetic association studies on candidate genes or at the genome-wide level. However, in many cases, the roles of these genes and their interactions in AD are still unclear. A comprehensive and systematic analysis focusing on the biological function and interactions of these genes in the context of AD will therefore provide valuable insights to understand the molecular features of the disease.

Methods and Algorithms: In this study, we collected genes potentially associated with AD by screening publications on genetic association studies deposited in PubMed. The major biological themes linked with these genes were then revealed by function and biochemical pathway enrichment analysis, and the relation between the pathways was explored by pathway crosstalk analysis. Furthermore, the network features of these AD-related genes were analyzed in the context of human interactome and an AD-specific network was inferred using the Steiner minimal tree algorithm.

Results: We compiled 430 human genes reported to be associated with AD from 823 publications. Biological theme analysis indicated that the biological processes and biochemical pathways related to neurodevelopment, metabolism, cell growth and/or survival, and immunology were enriched in these genes. Pathway crosstalk analysis then revealed that the significantly enriched pathways could be grouped into three interlinked modules–neuronal and metabolic module, cell growth/survival and neuroendocrine pathway module, and immune response-related module–indicating an AD-specific immune-endocrine-neuronal regulatory network. Furthermore, an AD-specific protein network was inferred and novel genes potentially associated with AD were identified.

Conclusion: By means of network and pathway-based methodology, we explored the pathogenetic mechanism underlying AD at a systems biology level. Results from our work could provide valuable clues for understanding the molecular mechanism underlying AD. In addition, the framework proposed in this study could be used to investigate the pathological molecular network and genes relevant to other complex diseases or phenotypes.

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