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Effects of Age, Sex, and Diabetes on the Transcriptome and Proteome Changes in the Brain after Cerebral Ischemia

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Abstract

This study investigates the effects of age, sex, and diabetes on transcriptome and proteome changes in the brain following cerebral ischemia. Utilizing a multidimensional approach, we integrate transcriptomic and proteomic analyses to elucidate the complex molecular landscape underlying stroke pathophysiology. Age-related alterations in gene expression and protein profiles are characterized by dysregulated pathways associated with inflammation, oxidative stress, and neuronal repair mechanisms. Sex-specific responses reveal distinct molecular signatures implicated in neuroprotection, neuroinflammation, and synaptic remodeling post-ischemia. Moreover, diabetes-induced modifications in gene and protein expression highlight perturbations in glucose metabolism, oxidative stress, and vascular dysfunction, exacerbating cerebral ischemic damage. By comprehensively delineating the interplay between age, sex, and diabetes in shaping brain molecular responses to ischemia, this study provides critical insights for personalized stroke management and targeted therapeutic interventions.

Keywords: Cerebral ischemia; Transcriptome; Proteome; Age; Sex; Diabetes; Stroke

Introduction

Cerebral ischemia, characterized by inadequate blood flow to the brain, poses a significant threat to neurological health worldwide. While its consequences are widely studied, the intricate interplay of age, sex, and diabetes in modulating post-ischemic brain alterations remains a complex area of investigation. Understanding how these factors influence the transcriptome and proteome changes in the brain following ischemic events is critical for developing targeted therapeutic interventions. This article delves into the multifaceted effects of age, sex, and diabetes on the molecular landscape of the brain post-cerebral ischemia [1].

Age-Related Transcriptomic and Proteomic Changes: Age exerts a profound influence on the brain's response to ischemic insult. Studies have revealed age-dependent alterations in gene expression patterns and protein profiles following cerebral ischemia. Older individuals often exhibit dysregulated expression of genes associated with inflammation, oxidative stress, and neuronal repair mechanisms. Concurrently, proteomic analyses have identified age-specific protein signatures linked to synaptic plasticity, neurodegeneration, and cell survival pathways. These age-related changes contribute to variations in ischemic stroke outcomes, including differential susceptibility to neuronal injury and recovery potential [2].

Sex Disparities in Brain Molecular Responses to Ischemia: Sex is a pivotal determinant of ischemic stroke incidence, severity, and recovery. Emerging evidence underscores the influence of sex hormones on the brain's molecular response to ischemic insult. Transcriptomic studies have elucidated sex-specific gene expression profiles, highlighting distinct signaling pathways involved in neuroprotection and neuroinflammation. Moreover, proteomic analyses have identified sex-specific protein networks implicated in synaptic remodeling, neuronal survival, and gliotic responses post-ischemia. The interplay between sex hormones, immune mediators, and neuronal signaling cascades shapes the sexually dimorphic outcomes observed in ischemic stroke [3].

Diabetes Mellitus

A modifier of brain molecular responses: Diabetes mellitus represents a major risk factor for ischemic stroke and exacerbates brain injury post-ischemia. Transcriptomic investigations have unveiled diabetes-induced alterations in gene expression related to glucose metabolism, oxidative stress, and vascular dysfunction, exacerbating cerebral ischemic damage. Proteomic profiling has further delineated diabetes-associated changes in protein abundance and post-translational modifications, highlighting perturbations in mitochondrial function, protein folding, and cell death pathways. The dysregulated molecular landscape in diabetic brains contributes to augmented neuroinflammation, impaired neurovascular coupling, and diminished regenerative capacity post-ischemia [4].

Integration and implications: Integrating age, sex, and diabetes into the analysis of post-ischemic brain transcriptomics and proteomics provides a comprehensive understanding of the molecular mechanisms underlying stroke pathophysiology. Unraveling age- and sex-specific molecular signatures offers insights into personalized stroke management strategies, facilitating the development of targeted therapies tailored to individual patient profiles. Furthermore, delineating the impact of diabetes on brain molecular responses to ischemia underscores the importance of glycemic control and vascular risk factor management in stroke prevention and treatment. Future research endeavors aimed at elucidating the dynamic interplay between age, sex, diabetes, and ischemic stroke will pave the way for precision medicine approaches in stroke care, ultimately improving clinical outcomes and enhancing quality of life for stroke survivors [5-6].

Study Design

This prospective observational study involves a cohort of

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ischemic stroke patients stratified by age, sex, and diabetes status. Patients presenting with acute ischemic stroke within a specified time window are recruited from multiple clinical centers. Baseline demographic, clinical, and imaging data are collected, including age, sex, medical history, stroke severity, and neuroimaging findings. Blood samples and brain tissue specimens are obtained from participants undergoing neurosurgical procedures or post-mortem examinations. Transcriptomic analysis is performed using next-generation sequencing techniques to profile gene expression patterns in brain tissue samples. Concurrently, proteomic analysis employing mass spectrometry enables the identification and quantification of protein abundance and post-translational modifications. Statistical analyses, including differential gene expression analysis, pathway enrichment analysis, and network analysis, are conducted to elucidate age-, sex-, and diabetes-specific molecular signatures associated with cerebral ischemia. Integration of transcriptomic and proteomic data facilitates a comprehensive understanding of the molecular mechanisms underlying stroke pathophysiology and provides a basis for personalized stroke management strategies. Ethical approval is obtained from the institutional review boards of participating centers, and informed consent is obtained from all study participants or their legally authorized representatives [7-8].

Conclusion

The effects of age, sex, and diabetes on brain transcriptome and proteome changes following cerebral ischemia are multifaceted and interdependent. By deciphering the molecular intricacies underlying these factors, researchers can advance our understanding of stroke pathophysiology and identify novel therapeutic targets. Integrating age- and sex-specific considerations into stroke research and clinical practice holds promise for personalized stroke management and improved patient outcomes in the era of precision medicine.

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Conflict of Interest

None

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