



DIFFERENTIAL GENE EXPRESSION BETWEEN THE CEREBELLUM AND PREFRONTAL CORTEX OF ALZHEIMER'S PATIENTS AND HEALTHY CONTROLS

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INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by memory loss, cognitive decline, and personality changes. AD is caused by the accumulation of amyloid-beta plaques and neurofibrillary tangles, resulting in neuronal damage and neuroinflammation, but the molecular mechanisms AD remain unclear [1, 2]. The prefrontal cortex (PFC) plays a key role in executive function and working memory. PFC connectivity is known to be detrimentally affected by AD [3]. The cerebellum, traditionally associated with motor control, is increasingly recognized for its contributions to cognition [4]. RNA-seq analysis in post-mortem brain tissue allows for differential gene expression between healthy controls and AD patients. Doing so provides greater insight into the potential molecular mechanisms that drive AD and potential therapeutic targets.

OBJECTIVE

This study aims to investigate how Alzheimer's disease differentially impacts gene expression in the prefrontal cortex and cerebellum by analysing RNA-seq data using principal component analysis (PCA) alongside a set of complementary bioinformatic and statistical tools, with the goal of identifying brain region-specific molecular signatures associated with the disease.

METHODOLOGY

We used the biostudies database for data acquisition ("Bulk RNA-seq of Postmortem Human Prefrontal Cortex and Cerebellum Brain Tissues" [5]. In R-studio we analysed the data and created the PCA and volcano plots. DESeq2 was used for differential gene expression analysis. The online tool gProfiler was used for functional gene set analysis.

PRINCIPAL COMPONENT ANALYSIS BETWEEN HEALTHY CONTROLS AND ALZHEIMER'S DISEASE PATIENTS

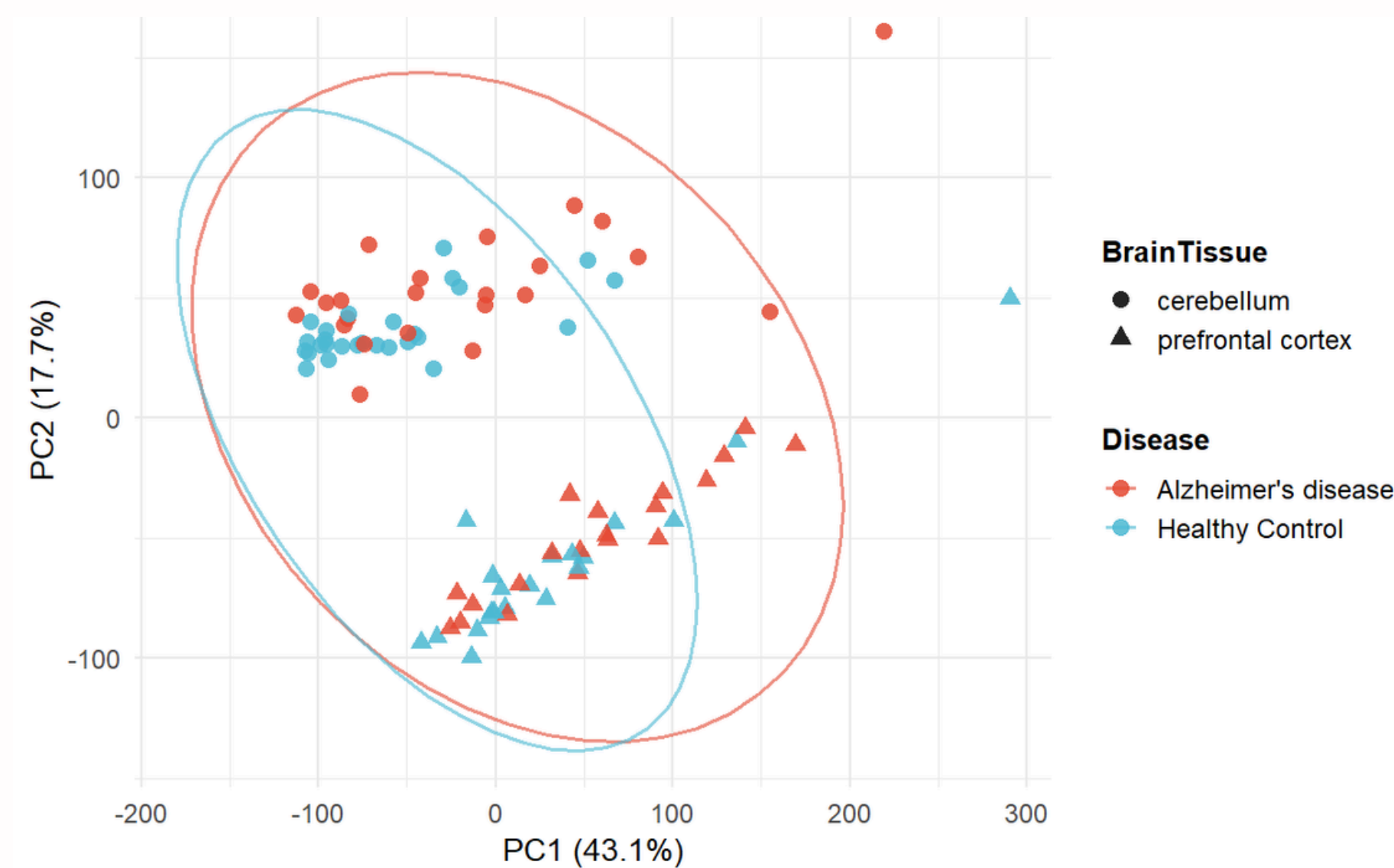


Figure 1. Principal component analysis (PCA) of RNA-seq data shows separation of Alzheimer's disease and control samples across brain regions. PCA shows distinct gene expression patterns between the cerebellum and prefrontal cortex. The first principal component explains 43.1% of the variance and the second principal component 17.7%. Neither principal component shows a difference between healthy controls and patients.

DIFFERENTIAL GENE EXPRESSION IN THE CEREBELLUM

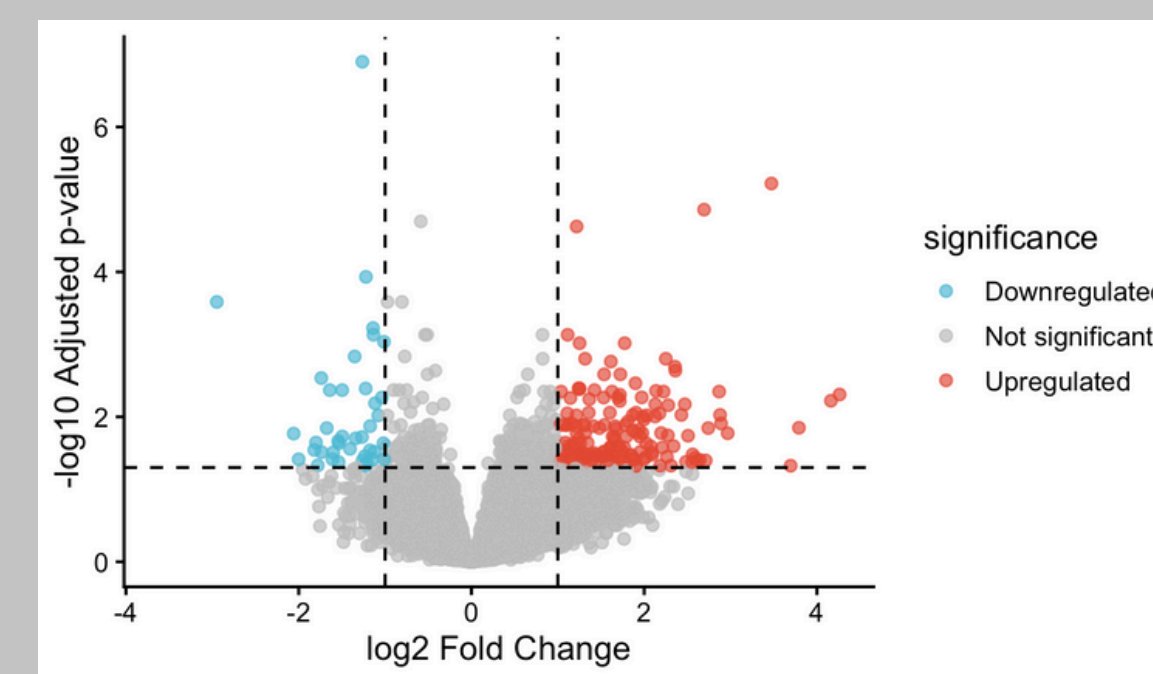


Figure 2. Volcano Plot of RNA-seq data shows significantly up- and downregulated genes in Alzheimer's disease in the cerebellum. The cerebellum of Alzheimer's disease patients shows many down- and upregulated genes compared to controls.

DIFFERENTIAL GENE EXPRESSION IN THE PREFRONTAL CORTEX

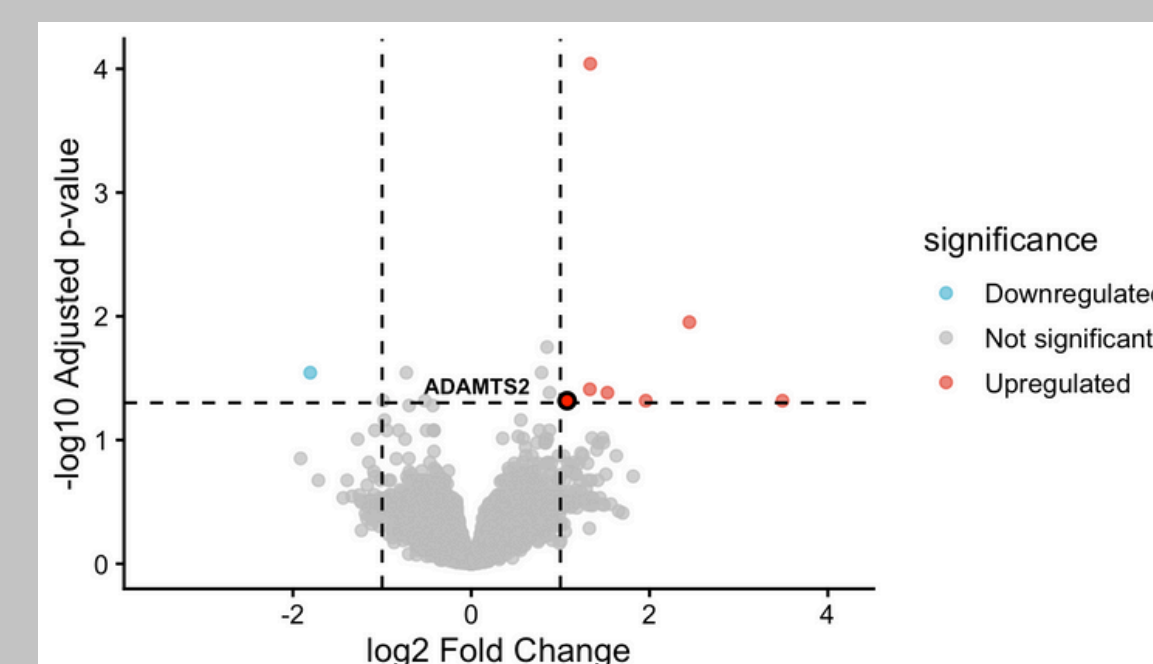


Figure 3. Volcano Plot of RNA-seq data shows limited significant up- and downregulated genes in Alzheimer's in the prefrontal cortex. The prefrontal cortex of Alzheimer's disease patients shows few down- and upregulated genes.

FUNCTIONAL GENE SET ENRICHMENT ANALYSIS

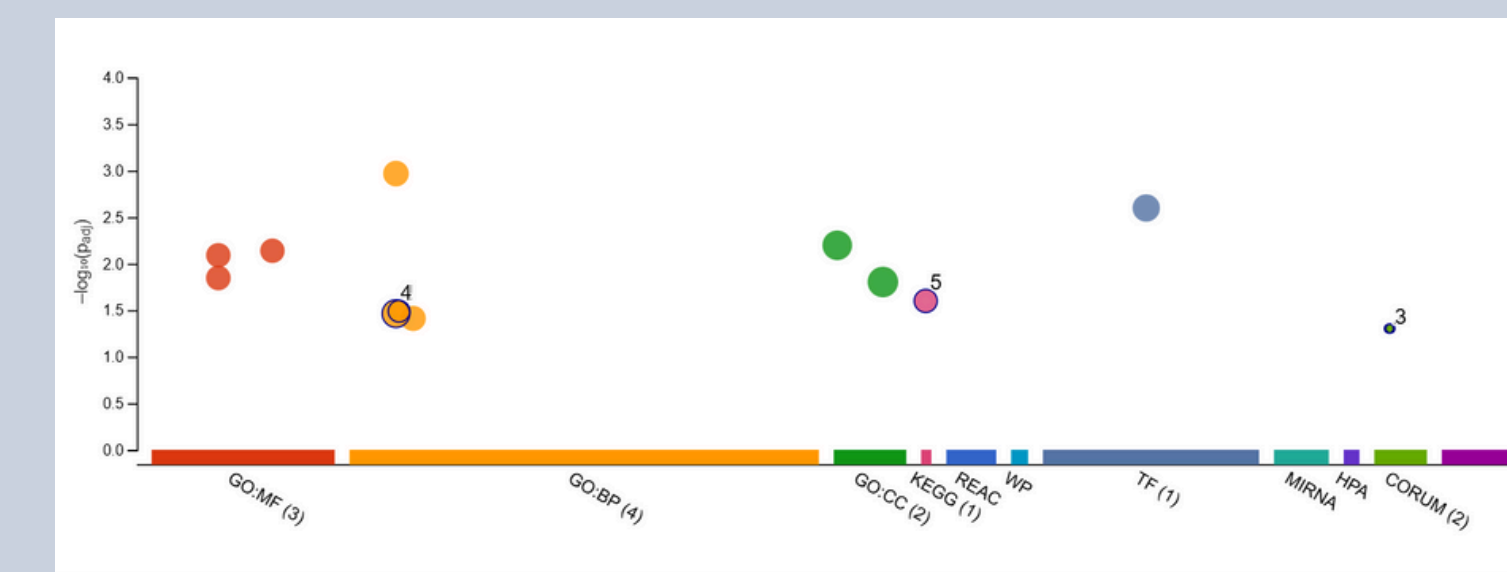


Figure 4. Functional profiling of upregulated genes in the cerebellum in Alzheimer's.

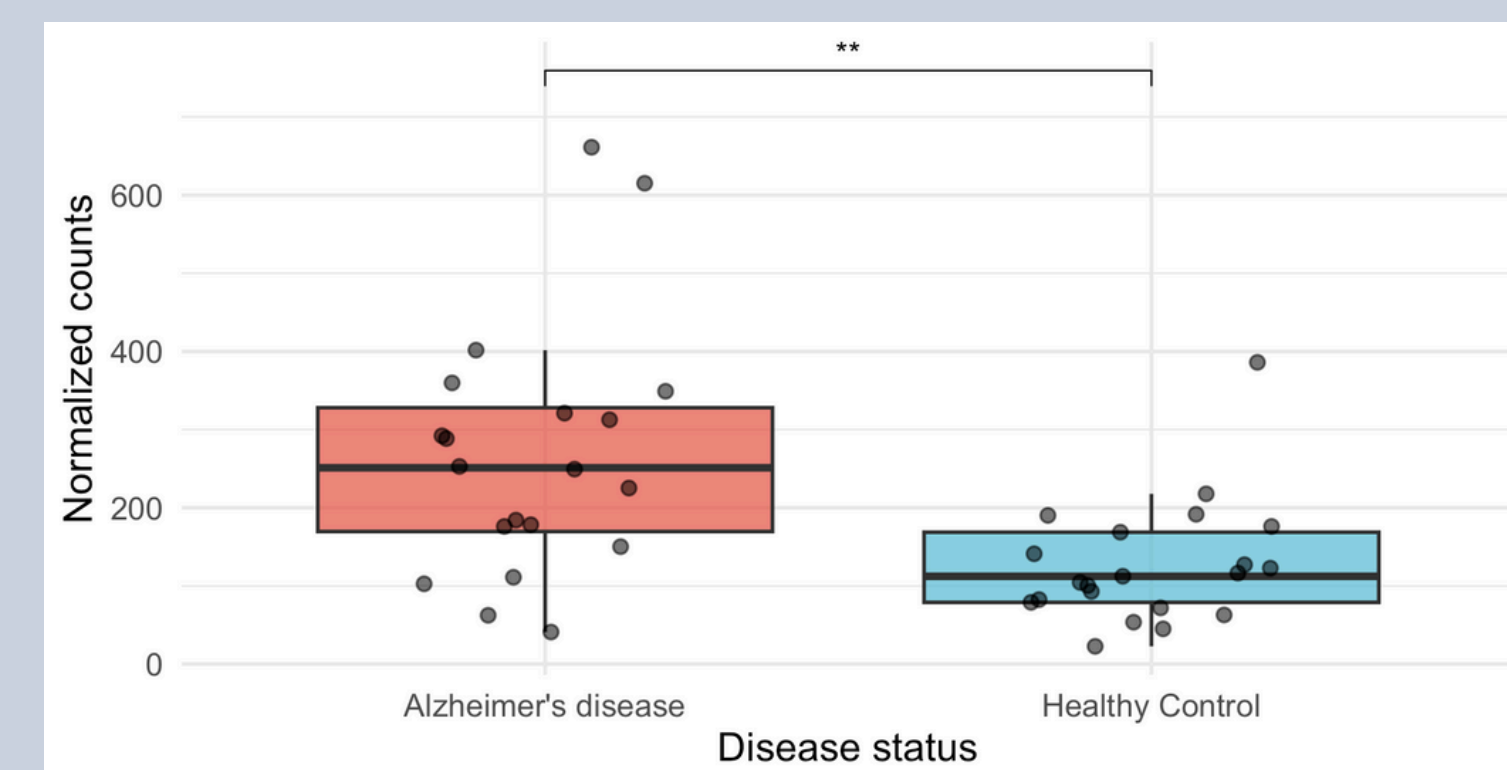


Figure 5: ADAMTS2 is upregulated in the prefrontal cortex of Alzheimer's disease patients compared to healthy controls. ** p < 0.01.

- Calcium signaling ↑ linked to synaptic dysfunction in AD [6]
- Immune receptors ↑ B-cell & cytokine complexes [7]
- Neuroinflammation ↑ defense response genes activated [7]
- ADAMTS2 expression ↑ Alzheimer's disease - role in extracellular matrix remodeling and neurodegeneration (Independent t-test: p = 0.0017) [8].

CONCLUSION

- The differential expression of genes is larger between the brain regions than between AD patients and controls.
- The cerebellum exhibits a significantly greater variation in gene expression compared to the prefrontal cortex.
- Genes related to neuroinflammation are upregulated in the cerebellum of AD patients and can therefore be potential drug targets.

SOURCES

