

Amygdala Gene Expression Under Death Circumstances

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Introduction

The amygdala is responsible for processing external stimuli and generating emotional responses. Particularly in response to fear, it is also capable of storing fear memories (1,2). Consequently, fear can also lead to physiological changes in the amygdala, such as gene expression (3). Therefore, we aim to investigate how a prolonged period of dying can impact gene expression in this brain region and identify common pathways affected by this process. To achieve this, data from the GTEx portal were retrieved, and the gene expression in the amygdala of patients who experienced a sudden death (group 1) was compared to those who had suffered a prolonged death (group 4). This research revealed that certain genes were upregulated in longer cases of death with variance in the affected transcription patterns based on age.

Material & Methods

Data from the GTEx Portal were used, including amygdala gene read counts and brain sample metadata (gender, age, cause of death, and sampled organs). The dataset was filtered to include only amygdala samples from individuals who experienced violent fast or slow deaths, and files were merged using donorID. Analyses were conducted in RStudio, generating a volcano plot, heatmap, and boxplots (see QR code for script).

Results & Discussion

Differential gene expression in the amygdala comparing violent, fast death to slow death.

The volcano plot for the differential gene expression showed us several up- and down-regulated genes. A literature review was conducted to gain a deeper understanding of the function of the most differentially expressed genes with the highest P-value. **IL1RL1** is a receptor activated by the cytokine IL-33, which is released from damaged cells, thereby initiating an early inflammatory response (4). During inflammation, **SERPINA3** is upregulated to counteract proteolytic activity and prevent tissue destruction (5). **KIF19** expression increases during prolonged cellular stress, as there is cytoskeletal remodeling and alteration of the cilia-based signaling to maintain structural integrity (6). Meanwhile, **ENSG00000281383**, a gene whose function is mostly unknown, is similar to YY1, suggesting involvement in histone deacetylation and acetylation (7,8).

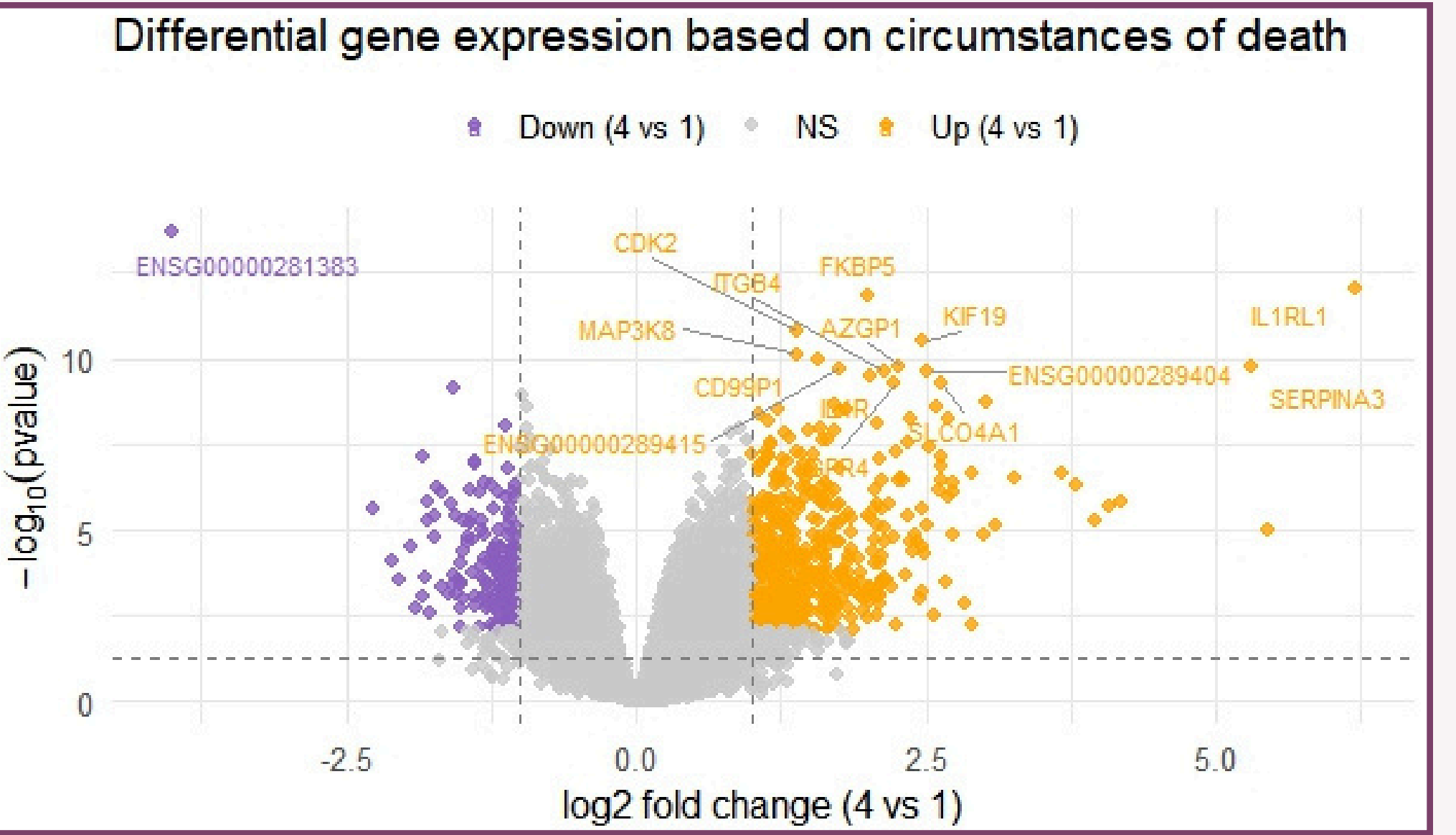


Figure 1: Volcano plot of differential gene expression in the amygdala when comparing violent and fast death to slow death. Colors indicate differential expression (fold change): purple = downregulation, yellow = upregulation. The threshold for log2fold change was set at -1 for downregulation and at 1 for upregulation. For the -log10(P-value), the threshold was set at 1. The most upregulated and significant genes are IL1RL1, SERPINA3, and KIF19, which are primarily involved in stress response and damage repair. The most downregulated gene is ENSG00000281383, for which the function is largely unknown; however, it is similar to YY1, suggesting involvement in histone acetylation.

Differential gene expression in the amygdala, comparing the z-score between different death circumstances.

Comparing the z-scores between violent and fast death versus slow death, several genes exhibit upregulation in violent and fast deaths. **ICRH** is a precursor to a neuropeptide hormone that is secreted to modulate homeostasis during stress (9). **HPCA** encodes a protein involved in phytosignal transduction and may reflect sensory/signal adaptation under stress (10). The function of **ENSG00000253553**, located on chromosome 8, is unknown. Meanwhile, genes such as MVP and TNFRSF6B are downregulated. These genes encode proteins that are involved in stress stabilization and cell survival (11,12).



Figure 2 : Heatmap of differential gene expression in the amygdala from individuals experiencing violent fast death (left) versus slow death (right). Colors indicate relative expression (Z-scores): purple = downregulation, yellow = upregulation. TNFRSF6B and MVP are upregulated in slow deaths, reflecting prolonged stress and survival signaling, while their downregulation in fast deaths suggests acute injury or cell loss. Neuronal genes such as HPCA and CRH show distinct patterns, highlighting altered neuroendocrine and stress-response activity between conditions.

Differential gene expression in sex and age

Other than speed of death, donors also differed in two other categories within the dataset, these being sex and age. To examine whether these other variables impact the differential gene expression between quick and long death conditions, a DGE analysis was performed on the groups individually. Genes with high differential expression and significance were then plotted to examine possible differences. Results showed that sex does not significantly impact DGE in both downregulated and unregulated genes. Age however did seem to have an impact, specifically, in the age range 70-79, far more genes were differentially expressed than in other age groups.

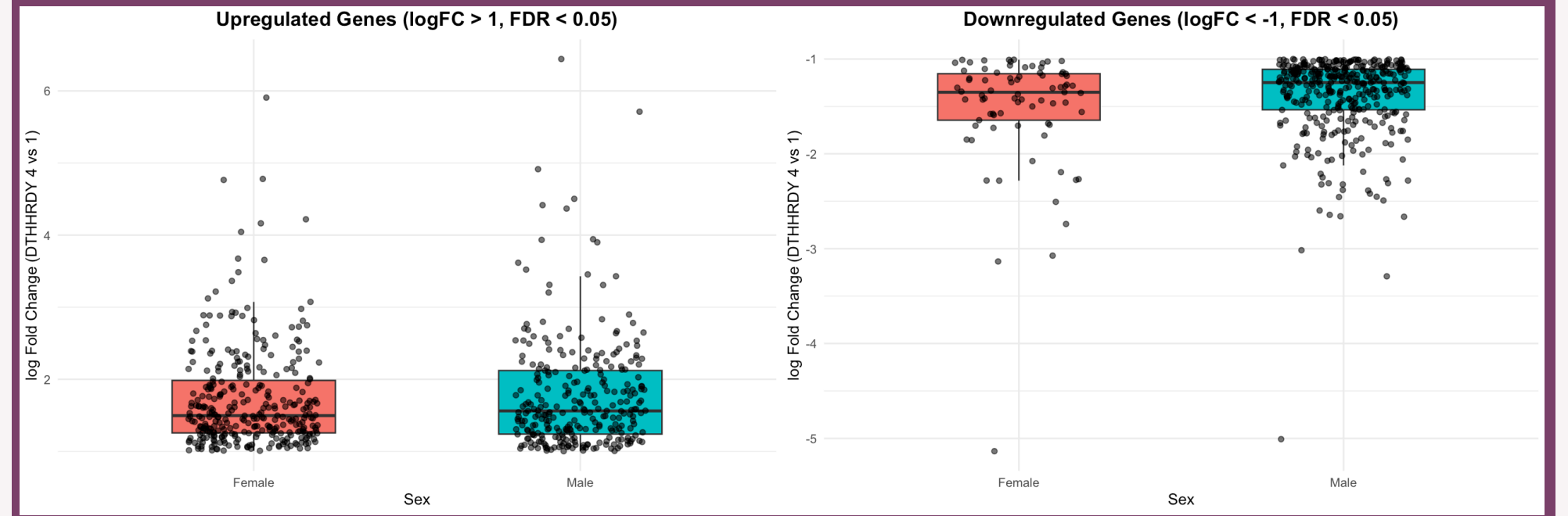


Figure 3A: Boxplots showing significantly differentially expressed genes ($|\log FC| > 1$, $FDR < 0.05$) between DTHHRDY 1 and 4 in males and females. Left plot shows upregulated genes, right plot shows downregulated genes.

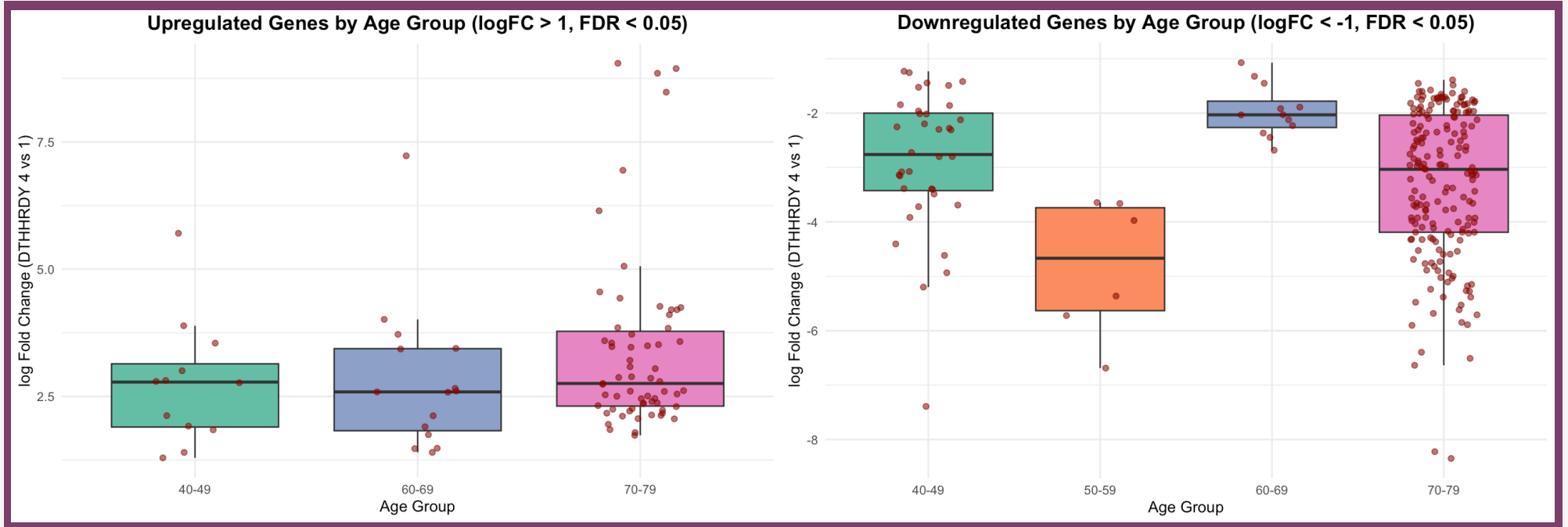


Figure 3B: Boxplots showing significantly differentially expressed genes ($|\log FC| > 1$, $FDR < 0.05$) between DTHHRDY 1 and 4 in varying age groups. Left plot shows upregulated genes, right plot shows downregulated genes. Age groups not represented on graph had no genes that passed the set thresholds.

Conclusion

Prolonged death appears to significantly alter gene expression in the amygdala, specifically in pathways related to stress, inflammation and cellular adaptation. The results of this poster show increased activity in genes involved in inflammatory signaling and cytoskeletal remodeling, alongside reduced expression of genes linked to cellular stability and survival. Age, but not sex, influenced these transcriptional patterns, with older individuals showing greater variability. These findings suggest that extended physiological distress causes characteristic molecular changes in the amygdala, highlighting the way prolonged dying impacts brain function at the end of life.