

FROM EMOTIONS TO THOUGHTS: HOW THE HUMAIN BRAIN IS WIRED

DIFFERENTLY ACCORDING TO SEX

Camilla Nedjari (S6459196), Roshni Esther Dutta (S4701712), Lotte Mulder (S4888626) ,
Berber Ziegns(S2957086), Emel Hyusein (S3820483), Derk Wiersma (S4897323)

TEAM 13

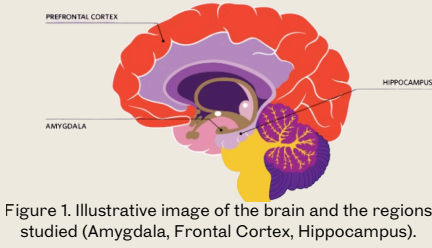
AIM

Investigate sex specific differences in gene expression across three brain regions, focusing on upregulated genes in females compared to males. This analysis provides insights into molecular mechanisms that may contribute to sex-based variability in brain function.

INTRODUCTION

The brain is a complex network of connected specialised regions.

- The amygdala, which plays a role in emotion processing, stress response, fear, and threat detection, shows distinct patterns of activation between males and females, often linked to sex-specific stress responses (1).
- The hippocampus, which is essential for memory formation, also exhibits structural and functional differences between sexes (4).
- Similarly, sex differences in the prefrontal cortex, which is responsible for cognition, decision making, social behavior, and motor control has been associated with estrogen signaling and its interaction with the amygdala (5).



GENE EXPRESSION

Differential Gene Expression: Female vs Male (Amygdala)

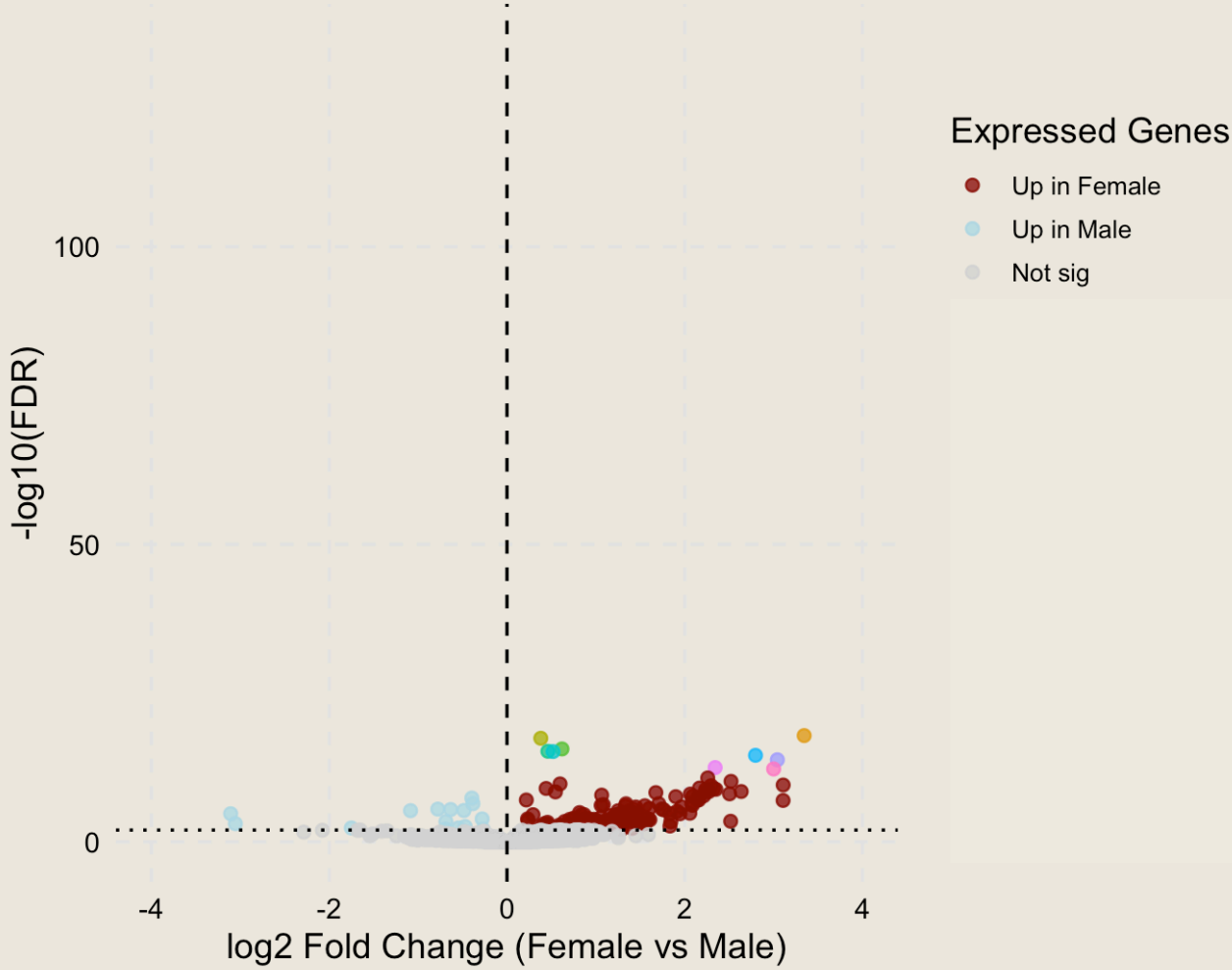


Figure 2: Volcano plot of the Differential Gene Expression in the Amygdala compared in males and females. This volcano plot shows the differential gene expression in the amygdala between males and females. Each point represents a single gene, with females' genes marked in dark red and the males' genes marked in light blue. The highest genes on the plot have greater significance. This volcano plot allows us to identify the genes with statistically significant gender differences in amygdala expression.

CONCLUSION

- We identified several significantly differentially expressed genes between males and females in the brain.
- Male upregulated genes were mainly located on the Y chromosome, as expected since females lack this chromosome.
- The dataset included approximately three times more male than female samples; however, our statistical methods were robust enough to account for this imbalance.
- False Discovery Rate (FDR) correction was applied to minimize false positives and ensure reliability.
- Later in the analysis, comparisons across brain tissues revealed a substantial overlap in differentially expressed genes, indicating consistent sex-linked expression patterns.
- A few non-sex-linked genes also appeared significant, possibly due to donor-related factors such as disease history or cause of death.
- The cohort ranged from 21–79 years, so age-related gene dysregulation may have influenced expression profiles.
- Some upregulated genes may play important biological roles, warranting further investigation into their effects on brain function and sex-based differences in health.

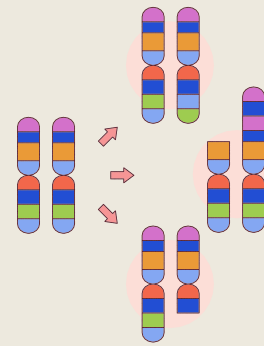
METHODS

- RNA-seq read count data and sample annotations for the amygdala, hippocampus, and frontal cortex were obtained from the GTEx database. The samples were grouped by sex (male and female).
- Genes with low expression (CPM < 1 in fewer than 3 samples) were removed. Normalisation and differential expression analysis were performed using the edgeR package, fitting a negative binomial model with sex as the main variable.
- Genes with a false discovery rate (FDR) below 0.01 were considered significantly differentially expressed. After which Ensembl gene IDs were mapped to gene symbols using biomaRt.
- Results were visualised using volcano plots, MA plots, PCA, and heat maps to explore overall expression patterns and sex-biased gene activity across the three brain regions.

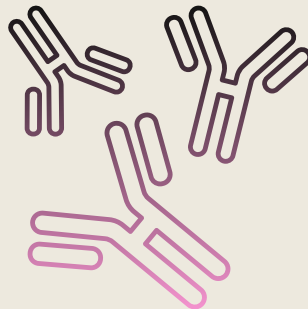
HIGHLIGHTS



TPO & IYD are related to Thyroid activity in females



ZFX affects neuronal development and gene regulation in females



IGKV4-1 related to Immunoglobulin variable region; antibody diversity in females

NLGN4Y nervous system development linked to ASD in males



RESULTS

