Analyzing Gene Expression Patterns In Associative Learning

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Introduction

- Located in the temporal lobe of the brain, the limbic system includes the Hippocampus and Amygdala which are associated with learning and memory.
- The Hippocampus is responsible for the processing and storage of short-term memory, long-term memory, and spatial navigation. Though the Amygdala is commonly known to be linked with emotions, fear, and anxiety, studies have proved its involvement in the modulation of memory consolidation.
- Purpose of this project is to analyze gene expression patterns for brain regions involved in the encoding, storage, learning, and retrieval of memories. Identify candidate genes for this behavior.

Methods

Gene expression data for the Hippocampus and Amygdala were collected from the Allen Brain Atlas (http://www.brain-map.org) using the differentially expression tool. Data was collected from four available donors.

Venny 2.1.8 (http://bioinfo.ccs.ceu.es/tools/venny) was used to compare the gene lists from four chosen brain donors to identify genes that are common and different across each donor.

Statistical analysis was done in PythonAnywhere (https://www.pythonanywhere.com) an online programming tool.

Cluster analysis and Gene Ontology classifications were obtained with DAVID (https://david.ncifcrf.gov/).

The STRING database (http://string-db.org/) was used to identify potential interacting partners, pathways, and other genes relating to associative learning using experimental data from gene studies.

GeneWeaver (http://www.geneweaver.org/) was also used to find further information for relevant genes.

Results

Gene Expression Profiling

The heat maps display raw expression data: fold expression of various genes in the Hippocampus and Amygdala from the profiles of four donors (H0351.2001, H0351.2002, H0351.1009, H0351.1012). Each column represents a tissue sample. This data is collected from rRNA that is co-expressed with GABA and hybridized to microarrays containing all human genes. Data with a fold change of >3 or above was used in the analysis. 5 genes are common between the two brain regions: NELLI, CARPT, FOSG1, GABRR, RCN2, STYL5, TRPC4

Two different sample types are used for comparison: the sample under study and the control. The heat maps range in color based on the score over a probe. Red areas of the heat maps indicate that the expression of the sample is greater than the control (a-score of >3 and above). Green areas show that the expression is less than the control (a-score of <3 and below). Black areas show that the expression is equal to the control (a-score of 0).

Common Genes

145 genes (93.7%) common in all donors

46 genes (10.2%) common in all donors

Statistical Analysis

Central tendency for Hippocampus. The distributions for the highest gene expression across all four donors are skewed to the right and clustered together near the (y-axis). For genes with a smaller fold change near the (x-axis). The mean fold change for each donor doesn’t vary much, approximately ranging from 4.4 - 4.7. The standard deviation values are close to the means indicating a large spread in the data. The lower fold change being approximately 1.9 and the highest being 2.3.

Conclusion

- The Gene expression patterns on the hippocampus for the Hippocampus are highly similar across all four donors whereas, for the Amygdala, it is more variable.
- The three common genes between four donors that were involved in the associative learning as NEUROD1, GRIN2B, and GABRA5. NEUROD1 is a transcription regulator for neuron differentiation. GRIN2B is a NMDA receptor subtype of glutamate-gated ion channels. GABRA5 is a subunit of a GABA receptor which is the major inhibitory receptor in the mammalian brain.

Amygdala results: There was no relationship found at this time for gene expressed in the Amygdala and learning/memory, although there are genes associated with broad range of neural processes that were found using an integrative genomics database.

Key References


Gene ontology (GO) was used to classify the common genes from the Venny graph. The (GO) term biological process (BP) were exclusively used to sole down genes of interest and genes that were relevant to the hippocampus. The gene report for associative learning provided three genes: GABRA5, GRIN2B, and NEUROD1.

Protein Interaction Network

There were 20 common genes expressed between two gene sets connected with associative learning.

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