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# Differential gene expression in young and old rats in response to chronic unpredictable stress

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*Motivation and Aim*: Aging and stress are known to significantly affect gene expression and physiological functions in mammals. However, the specific patterns of differential gene expression in response to stress across different age groups remain insufficiently studied. Our study investigates the impact of stress on gene expression in young and old rats, focusing on age-related differences in stress response pathways.

*Methods and Algorithms*: RNA sequencing was used to analyze gene expression profiles in two groups of rats (young and old) exposed to stress. Young (4 months) and old rats (12–14 months) were subjected to daily chronic unpredictable stress for 5 weeks, then samples of their hippocampus were sequenced. Differential gene expression analysis was performed, identifying genes with significant expression changes. Functional enrichment analysis (GSEA and GAGE) [1] was applied to uncover the biological processes and pathways affected by stress. Weighted gene co-expression network analysis (WGCNA) [2] was conducted to explore gene co-expression modules associated with age and stress response.

*Results*: A total of 202 differentially expressed genes (DEGs) were identified in old rats (12 UP and 99 DOWN) and 435 DEGs were found in young rats (201 UP and 234 DOWN). 55 common DEGs were observed between two groups, many of which were associated with ribosome function and protein synthesis, showing opposing trends in expression (upregulated in young and downregulated in old rats). WGCNA identified modules linked to ribosome activity, mitochondria and neurodegenerative diseases. Pathway analysis in young rats revealed increased activity of mitochondrial pathways and cortisol secretion regulation, while in old rats, there was a decrease in ribosomal activity, cell motility and oxidative phosphorylation pathways.

*Conclusion*: Co-expression analysis demonstrates the difference between age and stress factors in the studied groups of rats. Several clusters demonstrated differences between stressed and non-stressed animals related to translation functions, mitochondrial activity, cytoskeleton and PI3K signalling. Other clusters showed no clear association with age and stress, which may indicate false positives.

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