CHANGES IN HIPPOCAMPAL GENE EXPRESSION PROFILE FOLLOWING ACUTE AND CHRONIC STRESS IN THE MOUSE

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Exposure to stressful events leads to compensatory responses by an organism. However when the stressful stimuli are protracted they can lead to dysregulation of specific neurochemical mechanisms and to long-term changes in synaptic plasticity. Recently, several studies showed that stress changes the hippocampus structure and function. Here, to elucidate how acute and chronic stress affect the hippocampus function we used microarrays and screened the expression of > 10000 transcripts in the mice hippocampus. The stress was administered immobilizing the mice in restraint bags for 60 minutes. The acute and chronic stress was simulated in mice for 1 and 7 consecutive days, respectively. Animals were sacrificed at 3, 12 and 24 hours after restraint treatment. Control groups for both acute and chronic treatments were not subjected to the restrain procedure but were killed at the same times. The whole hippocampus was rapidly dissected and stored at -80C°. The RNA from each mouse hippocampus was extracted and the samples were hybridized onto CodeLink UniSet Mouse I BioArrays.
Differential gene expression analysis with a generalized linear model identified 270 statistically significant genes for acute stress whereas only 60 genes were identified for chronic stress. The differentially expressed genes were functionally annotated using Gene Ontology and KEGG categories. In the acute stress the larger gene expression changes was observed at 12 and 24 hours after the end of stress treatment. Functional analysis showed that these genes belong to different categories including neurogenesis, cell death, synaptic transmission, I-kappa B kinase/NF-kappa B cascade, neurotophic factor, transcriptional factor. In neurogenesis, the acute stress up regulates the expression of 3 genes: the Ciliary Neurotrophic Factor (CNTF), the Zinc finger protein 91 (Zfp91) and Fibroblast growth factor 12 (Fgf12). The genes regulated by chronic stress belong to three main functional categories: immuno response, regulation of biological processes and regulation of apoptosis. In particular, heat shock protein genes were generally found up regulated, while the Fibroblast growth factor was found down-regulated. Overall the results demonstrated that acute stress promotes gene expression changes aimed at protecting hippocampus neurons from damages. On the other hand chronic stress results in gene expression changes that suggest reduction in capacity of neurons to adapt to external perturbation and this may contribute to neurodegenerative processes occurring after repeated stress.