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Consequences of early life stress in mice: transcriptional and epigenetic hallmarks in frontal cortex and hippocampus

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Motivation and Aim: Stressing events in early postnatal period cause disturbances in neural connections and networks which lead to both direct and delayed effects on brain development.
Methods and Algorithms: We have investigated the influence of different types of early life stress – prolonged repeated separation of pups from their mothers for 3h per day or short-term repeated separation (15 min per day) during the first 2 weeks of life, and 24 h single maternal separation on 9th day of life.
Results: Short-term repeated separation led to some positive effects on behavior of mice, enhancing the social behavior and decreasing anxiety. Single separation resulted in decreased locomotor activity. Prolonged maternal separation led not only to changes of individual behaviors but also to deterioration of spatial memory and learning in Morris water maze and to impaired ability to recognize novel object. We detected the direct effects (on 15th day of life) of maternal separation on transcriptome in two brain regions – hippocampus and frontal cortex. In the frontal cortex, the stress negatively affected the axon ensheathment and myelination. In the hippocampus, downregulated genes were associated with NCAM interaction and signaling for neurite outgrowth. The analysis of distribution of H3K4me3 (ChIP-seq) in frontal cortex showed only some subtle changes in adult male mice with a history of early life stress.
Conclusion: Summing up, our data indicated that disturbances in expression of developmental genes may be mediated by alterations of epigenetic landscape which in turn may provide a basis for observed long-term effects of stress.
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