

SYNAPTOPROTEOMICS OF AN ANIMAL MODEL OF DEPRESSION COMBINING GENETIC VULNERABILITY AND EARLY-LIFE STRESS

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Depression is a severe and life-threatening disorder. This psychiatric illness affects 5-15% of the general population; its life-time prevalence is increasing and represents a major cause of disability, a great social burden, as well as an economic problem for public health system in most countries. Recent studies highlighted the important influence of environmental stress factors, such as adverse early life events, on an individual's genetic predisposition to develop mood disorders. Indeed, the experience of stressful events in childhood, such as neglect, abuse or parent loss, was found to increase the risk for the development of depression in adult life. The Flinders Sensitive Line (FSL) rats are a well validated animal model of depression carrying genetic vulnerability associated to distinct features of pathology. To reproduce early life stress events the FSL rats and their control, the Flinders Resistant Line (FRL) rats, were subjected to a maternal separation (MS) protocol (180 min/day from postnatal days 2-14). Treatment with the antidepressant (AD) escitalopram (ESC, 25 mg/kg/day) was carried out at weeks 11-14 of age. Many of the biological targets of AD are localized at synapses; thus to reduce the complexity of the proteome analyzed and to enrich for less abundant proteins, purified nerve terminals (synaptosomes) from prefrontal/frontal cortex (P/FC) and hippocampus (HC) of FSL and FRL rats were used. Synaptosomes from 8 rats per group were purified by Percoll gradients and analyzed by two-dimensional polyacrylamide gel electrophoresis (2DE). Statistical analysis of 2DE maps from P/FC synaptosomes revealed 37 proteins differently regulated in basal FSL vs. FRL rats. MS significantly dysregulated 48 proteins in FSL, and 24 proteins in FRL P/FC synaptosomes. Chronic ESC treatment differently regulated 33 protein spots in basal FSL, and 7 protein spots in FSL subjected to MS. Interestingly, in FSL rats 3 of the protein spots down-regulated by MS, were up-regulated by ESC treatment. Protein spots differently regulated in the various comparisons were excised from gels and identified by mass spectrometry analysis, by comparison with SwissProt and NCBI databases. In HC 2DE maps a number of protein spots up- and down-regulated in the various experimental groups were identified. Selected protein spots were excised and submitted to identification by mass spectrometry analysis. We report here the proteins identified in FSL vs. FSL-MS vs. FSL-MS-ESC comparison, belonging to different classes including proteins of pre- and postsynaptic machinery.

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