Functional/structural remodeling induced by behavioural stress at excitatory synapses: implications for pathophysiology and treatment

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Everybody is exposed to stress during daily life but why do some individuals develop stress-related disorders, whereas others adapt well? The impact of stress on emotional and cognitive behavior varies depending on the type of stressor, its intensity and duration, the gender of the individual, the time window of development at which the stress exposure occurs. The outcome of stress ranges from plasticity enhancing effects and improved cognition, when stress response is efficient, to noxious effects, when the response is overused. A maladaptive stress response can lead to epigenetic changes, impaired brain functions and may ultimately trigger the development of neuropsychiatric disorders. Thus, the identification of neural mechanisms underling resilience and vulnerability to stress is of crucial importance in the understanding of neuropsychiatric disorders pathophysiology and in the development of improved treatments.

Laura Musazzi, one of the winners of the SIF prizes 2014 financed by Otzuka, working in the laboratory headed by Prof. Popoli (Laboratory of Neuropsychopharmacology and Functional Neurogenomics at the Dipartimento di Scienze Farmacologiche e Biomolecolari, Università degli Studi di Milano), contributed to dissect the effects of acute stress at excitatory synapses in the prefrontal cortex. In particular, they have previously showed that acute stress rapidly enhances excitatory (glutamatergic) transmission in prefrontal cortex, together with an increase in the number of docked vesicles and small excitatory synapses, and that chronic treatment with antidepressants attenuates these effects (PLoS One, 5(1):e8566, 2010; Mol. Psy., 19:433-443, 2014; Int J Neuropsychopharmacol., 18(3), 2014). They have also shown that the increase of trafficking into the readily releasable pool of glutamate vesicles induced by acute stress is dependent on synaptic, non-genomic action of glucocorticoids. They are now studying the time-dependent effects of acute stress and of chronic stress on prefrontal cortex structural and functional plasticity and related cognitive behavior. The different glutamatergic modifications in functional and morphological plasticity suggest a biphasic process, during which the stress response in prefrontal cortex may turn from early increased excitatory activation into its opposite. The identification of these points and the players involved in the switch are crucial for the understanding of the dynamics of stress-related pathology.