Acute stress induces area-specific changes in glucose metabolism in rat brain

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Stress is recognized as a main risk factor in the etiopathogenesis of neuropsychiatric disorders (Popoli et al., 2012). The stress response is a physiological mechanism of adaptation essential for survival but, when the stressful event is prolonged or overwhelming, maladaptive mechanisms could occur, thus increasing the risk to develop a stress-related pathology. A consistent body of literature shows that acute stress can induce rapid adaptive changes in neuronal circuitry, influencing the release of neurotransmitters, circulation of cytokines and hormone secretion. These alterations allow to activate the so called 'fight-or-flight response', which is essential to survival in a threatening environment. In this context, it is conceivable that energy metabolism and mitochondrial activity are deeply affected by stress. Since energy produced by mitochondria actively regulate synaptic transmission, brain is vulnerable to bioenergetic fluctuations and mitochondrial defects induced by stress (as a review see Picard and McEwen, 2014). Glucose is the main energy source for the adult brain, and it is required in the synthesis of neurotransmitters, including glutamate and ϒ-aminobutyric acid (GABA).
Main aim of the present study was to evaluate the effect of acute foot shock (FS) stress on brain glucose metabolism in rats. The recent progress in neuroimaging techniques, such as Positron Emission Tomography (PET), make possible to appreciate in vivo brain area-specific alterations of metabolism, leading to a better understanding of how brain responds to stressors and which cerebral areas are involved in this mechanism. We employed [18F]FDG-PET techniques on FS-stressed rats to measure changes in brain glucose metabolism induced by acute stress. Our results showed an increase of energy consumption in rostral regions, including primary and secondary motor cortex and prefrontal cortex, and the anterior part of olfactory nucleus, endopiriform nucleus, piriform cortex, striatum and dorsal hippocampus. On the other hand, acute stress induced a decrease in glucose metabolism in ventral regions such as thalamus, hypothalamus and ventral regions of hippocampus. Moreover, to understand whether these changes were related to modifications in synaptic function, we also assessed changes in synaptic glucose metabolism. To this aim, we analyzed enzymatic activity of hexokinase, the rate-limiting enzyme for glycolysis in the brain, in purified synaptosomes from selected brain areas of control and stressed rats. Consistently, hexokinase activity resulted to be increased by acute stress in synaptosomes from prefrontal cortex and dorsal hippocampus while showing an opposite trend in those from ventral hippocampus.
Taken together, these results suggest that acute stress increases energy consumption (i.e. activation) of rostral brain areas and exerts the opposite effect in more caudal regions. This is in line with previous studies reporting increased functional plasticity after acute stress in selected brain areas, including prefrontal and frontal cortex and dorsal hippocampus (Joëls et al., 2009; Musazzi et al., 2015).

Popoli et al. (2012) *Nat Rev Neurosci.* 13(1), 22-37
Picard and McEwen (2014) *PNAS* 111(1), 7-8
Joëls et al. (2009) *Nat Rev Neurosci.* 10(6):459-66
Musazzi et al. (2015) *Front. Psychiatry* 6, 60-70