SEROTONIN STIMULATES MICE SKELETAL MUSCLE 6-PHOSPHOFRUCTO-1-KINASE THROUGH TYROSINE-PHOSPHORYLATION OF THE ENZYME ALTERING ITS INTRACELLULAR LOCALIZATION.

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Serotonin (5-HT) is implicated in regulation of many physiological and pathological events. Among the most intriguing properties of 5-HT are the ability to up-regulate mitosis and to stimulate glucose uptake and consumption on skeletal muscle. The aim of this study is to gain further insights in the mechanisms involved in the control of glucose metabolism, mediated by 5-HT, on mice skeletal muscle homogenate. Here we show that 5-HT promoted a dose-dependent activation of the key regulatory glycolytic enzyme 6-phosphofructo-1-kinase (PFK), which was maximal activated with 25 pM 5-HT (2.5-fold compared to control). The 5-HT effects observed involves the activation of 5-HT_{2A} receptor, since it is prevented by spiperone. Additionally, 5-HT induced tyrosine-phosphorylation and activation of PFK was prevented by genistein, a tyrosine kinase inhibitor. No serine-phosphorylation of PFK was observed in the presence of 5-HT. Serotonin increases the binding of PFK on muscle cytoskeleton, an effect probably due to the tyrosine-phosphorylation of the enzyme. Wortmannin did not alter the activation of PFK by 5-HT, showing that these effects involves a non-insulin dependent pathway. Altogether, our experiments show evidence of a tyrosine pathway involved in the control of glucose metabolism in skeletal muscle, promoted by serotonin.

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