(*The FASEB Journal.* 2006;20:A393)

236.29

Effect of creatine on protein synthesis in differentiating myogenic cells

Louise Deldicque[1], Daniel Theisen[1], Luc Bertrand[2], Louis Hue[2] and Marc Francaux[1]

[1] Université catholique de Louvain, Place Pierre de Coubertin, Louvain-la-Neuve, 1348, Belgium,
[2] Université catholique de Louvain, Avenue Hippocrate, Brussels, 1200, Belgium

ABSTRACT

The purpose of this study was to determine whether creatine (Cr, 5mM) is able to increases protein synthesis in myogenic C_2C_{12} cells and to identify the signalling pathway(s) involved in this putative stimulation. Cr increased protein synthesis as measured by a larger incorporation of labelled [^{35}S]methionine into both sarcoplasmic and myofibrillar proteins ($P<0.05$). Moreover Cr promoted the fusion of myoblasts since Cr increased the number of nuclei within myotubes by 20% after 96h of differentiation ($P<0.001$). To elucidate the signalling pathway induced by Cr, we first analyzed some protein markers affected by Cr. At 96h of differentiation, Cr enhanced the expression of myosin heavy chain-II ($P<0.01$), troponin T and titin ($P<0.05$) but neither citrate synthase nor lacticodehydrogenase. Because we had previously reported that Cr increased IGF-I mRNA, we analyzed the effect of Cr on calcineurin, PI3K and MAPK pathways. The inhibition of calcineurin by cyclosporin A and ERK-MAPK by PD098059 did not repress the hypertrophic effect induced by Cr indicating that these two pathways are probably not involved. On the other hand, the inhibition of p38 by SB202190 and mTOR by rapamycin completely inhibited differentiation and Cr did not reverse this effect indicating that the p38-MAPK and the mTOR pathways could be implicated in the hypertrophic effect induced by Cr. Moreover, after 3 days of differentiation, Cr enhanced the phosphorylation state of Akt/PKB, GSK3, mTOR and $p70^{s6k}$ ($P<0.05$). Cr also affected the phosphorylation state of p38 and the nuclear expression of MEF2. This study points out the involvement of both Akt/PKB and p38-MAPK pathways in the hypertrophic effect induced by Cr in $C2C_{12}$ cells.