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Effect of high-dose creatine supplementation on endogenous creatine synthesis during exercise

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Creatine (Cre) has become one of the most popular ergogenic sport supplements used today[1,2]. Cre supplementation can improve athletic performance and cellular bioenergetics[3]. A routine oral Cre protocol recommended for humans is a loading dose of 20 g/d (0.3 g/kg/d, 67 kg body weight) for 5–7 days, followed by a long-term maintenance dose of 2–5 g/d (0.03–0.075 g/kg/d)[4]. The doses of 1.5 g/kg/d and 0.15 g/kg/d for rats were calculated from the recommended loading dose of 20 g/d (0.3 g/kg/d) and the maintainable dose of 2 g/d (0.03 g/kg/d) for human subjects[4] according to Calabrese[5]. Thus the amounts of 1.5 and 6.0 g/kg/d Cre were considered to be high- or higher-dose in the rat study. The L-arginine:glycine amidinotransferase (L-AGAT) in kidneys is regarded as a key enzyme in the endogenous Cre synthesis in mammals, and the guanidinoacetic acid (GAA) is the precursor in this synthesis. The aim of the present study was to determine the effect of supplementation with 0, 1.5 and 6.0 g Cre /kg body weight per day for 2 weeks on the L-AGAT activity in the kidneys, the GAA concentration in the livers, and serum Cre and creatinine in swim-trained male Sprague–Dawley rats. L-AGAT activity and the GAA concentration were determined spectroscopically. Cre and creatinine in serum were also measured using an autoanalyser (7170A Hitachi Ltd., Japan). Treatment groups rats ($n = 10$ per group) were trained to swim for 2 h/d and 6 days/week for 2 weeks. The control group rats (without Cre supplementation, $n = 10$) were sedentary for 2 weeks. In the comparison between the swim-trained group without Cre supplementation and the control group, L-AGAT activity and GAA concentration in the swim-trained group increased (%) by 15.4 ($P<0.01$) and 26.7 ($P<0.01$). In three swim-trained groups, the L-AGAT activity and the GAA concentration decreased (%) by 61.7 ($P<0.01$) and 69.7 ($P<0.01$), and 16.6 ($P<0.01$) and 45.8 ($P<0.01$), respectively, in the groups supplemented with 1.5 and 6.0 g Cre/kg per day for 2 weeks compared to the group without Cre supplementation. Serum Cre and creatinine concentrations in the group receiving 6.0 g Cre/kg per day increased significantly. L-AGAT activity was positively correlated with the concentration of GAA ($n = 30$, $r = 0.84$, $P<0.001$); however, negatively correlated with serum Cre ($n = 30$, $r = 0.72$, $P<0.001$). These results indicate that in rats L-AGAT activity and GAA concentration could be markedly enhanced by exercise, implying that exercise may benefit endogenous Cre synthesis due to more Cre needed during exercise. The L-AGAT activity and GAA concentration, however, could be rapidly reduced by supplementation with 1.5–6.0 g Cre/kg per d, which is equivalent to 20–80 g Cre/d (67 kg body weight) in human subjects[5], suggesting that high-dose Cre supplementation may result in depression of endogenous Cre metabolism and may have potential adverse effects on the exercise-trained body. Little is known about the effect of high-dose Cre supplementation on the immune system; the results of a follow-up study of immune function will be of interest.

1. Koenig CA, Benardot D, Cody M *et al*. 2008) *J Strength Cond Res* **22**, 1081–1086.
2. Schoch RD, Willoughby D & Greenwood M (2006) *J Int Soc Sports Nutr* **3**, 60–66.
3. Harris RC, Söderlund K & Hultman E (1992) *Clin Sci* **83**, 367–374.
4. Hultman E, Söderlund K, Timmons JA *et al*. (1996) *J Appl Physiol* **81**, 232–237.
5. Calabrese EJ (1991) *Principles of Animal Extrapolation*, pp. 499–527. Chelsea, MI: Lewis Publishers Inc.