Creatine Increases Satellite Cell Activity and IGF-1 mRNA in Skeletal Muscle.

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Creatine (Cr) is the most popular nutritional supplement on the market, with yearly sales over $400 million1. The reason for its popularity is simple: it works! As you probably have read for the hundredth time...Cr is formed by combining the amino acids glycine, arginine, and methionine and is produced in physiologic amounts by the liver, kidneys, and pancreas2. In addition to natural synthesis, Cr is also found in protein-rich sources such as meat and fish. The total daily requirement of Cr is 2 g/d, approximately half of which comes from in vivo production and the other half from dietary sources3. The effects of oral Cr supplementation on contractile performance and metabolism of skeletal muscle recently have become an area of major interest in exercise physiology. Cr not only increases work performance but has recently been shown to increase muscle hypertrophy thru activation of satellite cell activity and increasing mRNA IGF-1 activity. The evidence has accumulated over the last several years showing that Cr intake can elevate muscle Cr stores and improve one's capacity to perform maximal intermittent exercise such as resistance exercise 4, 5 but has no effect on endurance type of exercises7.

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Creatine Uptake...A
Little Bit Goes a Long Way!

With Cr supplementation, a little bit goes a long way. The research suggests that 3-5 grams is sufficient, some researchers suggest a even lower dosage depending on the amount of dietary creatine consumed yet the exact dosage remains to be determined...anything more than that is not going to give additional gains. In fact the bulk of Cr ingested at high dosage is excreted in the form of urinary Cr. Nobody likes pissing money down the drain..so low dose Cr is the way to go. First, during dietary Cr supplementation, Cr accumulation is most pronounced in those individuals with the lowest initial Cr stores. When Cr was tested on vegetarian athletes, they made huge gains in strength because they consumed low endogenous dietary Cr. Dietary sources include beef, tuna, cod, salmon, herring, and pork. The normal dietary intake of creatine is 1-2 g/day, although vegetarians may consume less. Basically, individuals with the lowest starting intracellular Cr levels would be expected to have the highest initial Cr uptake rates. Consumption of Cr supplementation results in high intracellular rates that should rapidly expand the intracellular Cr pool. So what about bodybuilders whom consume large dietary sources of Cr that give an adult T-REX a run for his money? Individuals with initially high intracellular creatine [Cr]i would not be expected to exhibit the marked increase in Cr uptake rate as for the individuals with low initial [Cr]i. In addition, the Cr uptake rate could be downregulated with a sustained extracellular Cr load when [Cr]i is normal or elevated, although this is reported only in the fast twitch muscle since fast twitch muscles contain the highest source of [Cr]i.

When a bodybuilder first starts consuming Cr, accelerated uptake of Cr appears to occur initially, followed by a decline, possibly related to a decline in Cr transporter (CrT) number and the modulation of CrT activity associated with an increased [Cr]i8. It's not necessary to take a lot as the Cr uptake capacity differs among skeletal muscle fiber types. I would not worry about choosing a more expensive protein powder because it has Cr added to it, especially since after reading the article bodybuilders should be encouraged to be consuming low dosage Cr supplementation. It's interesting that although type II b fibers explosive muscle fibers store more Cr than slow oxidative type I fibers, its interesting that one study reported that in rats whom were supplemented Cr for a few days the rates of Cr uptake were greatest in the slow-twitch muscle fibers and less in the fast-twitch type II fibers. It is interesting the study that noted the Cr

uptake rates were inversely related to the total resting Cr concentration within the fiber types. Regardless of the absolute value obtained under various experimental conditions, Cr uptake by the soleus muscle (a slow twitch fiber) was generally 45-70% greater than the uptake by the white gastrocnemius muscle (a fast twitch fiber). The greatest Cr uptake rate was observed in the fiber type with the smallest Cr content (soleus), whereas the opposite was true for the white gastrocnemius with the largest Cr content. Thus the fiber type with the highest Cr total content exhibits the lowest uptake rate. Strikingly, the Cr content of the soleus is ~40% less than that of the white gastrocnemius muscle. Curiously, the increase in Cr uptake was observed in the high-oxidative fiber sections that possess relatively high mitochondrial contents and the cell fraction identified by Walzel and coworkers that contain the vast majority of the Cr transport proteins9. Based on the research low dose Cr supplementation is the way to go as fast twitch muscle fibers which contain the greatest potential for muscle hypertrophy can only store a limited amount, thereafter it's either excreted or shuttled into slow oxidative fibers.

Creatine Increase
Muscle Hypertrophy

It has been reported that short-term Cr intake increases fat-free mass in strength-trained athletes10,13. Accordingly, some in vitro (test tube) findings indicate Cr stimulates the biosynthesis of muscle myosin11,12. In mice that are genetically engineered to be Cr deficient, the mice have increased muscle damage, decreased muscle mass, and reduced voluntary exercise capacity19. Decreased force developed per unit cross-sectional area by skeletal muscle of Cr deficient mice are due in part to decreased myofibrilliar and increased mitochondrial content, which may participate in muscle weakness. Indeed, a decrease in total myosin heavy chain of 25% in gastrocnemius and 45% in soleus was also described in Cr deficient engineered mice18.Cr is also being recognized as supplement to benefit patients with neurodegenerative and muscle wasting disorders14. So how exactly is Cr increasing muscle hypertrophy?
At first, it was suggested that the increase in muscle mass after short-term Cr supplementation were due to fluid retention20 but later studies over longer periods taking muscle biopsies documented true increases in muscle fiber area15,25.
Cr has no effect on increasing muscle protein synthesis but reduced muscle protein breakdown was observed in men16, 17, 24. New studies have recently been published which have shown that Cr does a whole lot more than just increase work capacity.

Creatine Increases IGF-1
mRNA Activity and Satellite Cell Activation.

New studies have been published
which is turning new and novel mechanisms for Cr increases muscle mass. One of the ways Cr may be increasing muscle
hypertrophy is thru increasing IGF-1 mRNA.
Among the known growth factors, IGF-1 is known to stimulate satellite
cell activity as well as protein synthesis, as well as increasing muscle hypertrophy.
In fact, IGF-1 is such a potent stimulator of muscle hypertrophy that infusion
of local IGF-1 directly to skeletal muscles has shown increases muscle mass22.
It was earlier reported that when muscle cells were cultured in test tubes, the
addition of Cr resulted in improved cell differentiation and increased expression
of IGF-1 mRNA21. So what about human studies? Human studies have also shown that Cr
supplementation increases mRNA IGF-1 activity as well. In a double-blind cross-over design, muscle biopsies
were taken from the vastus lateralis of resistance trained men at rest and 3
and 24 hours post exercise who had taken Cr or a protein /carbohydrate drink
for 5 days. After Cr supplementation,
resting muscle expressed more mRNA for IGF-I (+30%). Exercise also caused
an increase by 3 h postexercise in IGF-I (+24%) and by 24 h postexercise in
IGF-I (+29%), but this effect was not increased by Cr supplementation. It's
interesting that in the study, Cr increased mRNA IGF-1 activity without
exercise, but taking Cr and exercise did not augment the response. The researchers concluded that the increase
in lean body mass often reported after Cr supplementation could be mediated by
signaling pathway(s) involving muscle mRNA IGF-123.

In
exercised muscle, a great deal of attention has been focused on IGF-I through
its effects on increasing protein (sarcomere) formation. An increase in IGF-I
is seen in muscle after acute maximal eccentric bouts of exercise. Local production of IGF-I undoubtedly
stimulates the growth of postnatal muscle and an increase in muscle mass. mRNA
for IGF-I is seen in myoblasts (i.e. satellite cells) and myotubes in vivo in
injured muscle, and the pattern corresponds closely to that for satellite cell
activation. As you probably are aware,
mRNA IGF-1 increases muscle hypertrophy primarily thru activating satellite
cell activity. In a recent issue of the Journal of Physiology a new study was
published that reported that Cr can also increase satellite cell activity. In that study, in a double-blinded design 32
healthy, male subjects were assigned to strength training for 16 weeks while
receiving either Cr, protein, or a placebo. Muscle biopsies were obtained at
week 0, 4, 8 (week 8 not CON) and 16 of resistance training (3 days per week). Results of the study concluded that all
training regimes were found to increase the proportion of satellite cells, but

significantly greater enhancements were observed with Cr supplementation at week 4 and at week 8. Furthermore, Cr supplementation resulted in an increased number of myonuclei per fiber and increases of 14-17% in muscle fiber area at week 4, 8 and 16. In contrast, the protein drink group showed increase in muscle fiber area only in the later (16 week, +8%). This study is pretty important to bodybuilders in that it's the first study that shows Cr supplementation in combination with strength training amplifies the training-induced increase in satellite cell number and myonuclei concentration in human skeletal muscle fibers, thereby allowing an enhanced muscle fiber growth in response to strength training.

In conclusion, Cr supplementation affords a scientifically proven means of improving performance and increasing muscle hypertrophy during exercise of high to maximal intensity. Cr supplementation has the potential to benefit all bodybuilders engaged in training that involves repetitive bouts of high-intensity exercise. The increased training load that could be tolerated by bodybuilders might be greatly beneficial to their eventual competitive performance. Additionally, Cr is probably about one of the cheapest supplements that actually improves muscle hypertrophy.

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