Proton MRS of the brain following oral creatine supplementation

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Introduction: Although not demonstrated in all studies, there are published data that show a reduction in muscle fatigue with dietary supplementation of creatine (Cr). Under controlled conditions, oral supplementation can enhance sporting performance (1). One suggested mechanism is that an increase in intra-muscular concentration of Cr provides a phosphate buffer for the synthesis of ATP: the provision of this buffer increasing the ability to perform exercise. The use of Cr supplementation in sport is common practice. However, it is controversial: there is a lack of data relating to health issues surrounding chronic use. As in muscle metabolism, Cr provides a vital phosphate buffer in brain metabolism and it would thus seem important to investigate the effects of supplementation on the brain. This study sought to investigate the cerebral metabolic effects of dietary Cr supplementation, depicted on spatially-localised, proton MR spectroscopy (H-MRS).

Methods. *Study population:* Eighteen male sport and exercise science students and other competitive sportsmen (mean ± standard deviation from the mean): age 22.7 ± 1.3 years, stature 178.0 ± 6.3cm and body mass 80.6 ± 6.7kg participated in this study. *Cr supplementation:* In a double-blind trial, 12 subjects consumed 20g·day^{-1} of Cr monohydrate for 5 days, administered as 5g boluses taken 4 times per day. Each bolus was dissolved in 200 ml of orange juice. The remaining 6 volunteers ingested a placebo powder (maltodextrin) disguised in the same way. *MR:* The participants were scanned twice: on the days before and after the oral ingestion period. H-MRS was performed at 1.5T (Eclipse, Philips Medical Systems). Spectra were obtained from a single cubic volume of interest (8 ml) placed within predominantly deep frontal white matter (fig 1). Two spectra were acquired from each subject at both scan episodes: (i) one at short TE / long TR (20ms/3000ms) using a stimulated echo acquisition mode (STEAM) technique; and (ii) one at long TE / intermediate TR (135ms/1600ms) using a point resolved (PRESS) spin-echo technique (fig 1). Results obtained at short TE were expressed as the areas under the Choline (Cho), Creatine (Cr) and N-acetyl (NA) resonances relative to that of unsuppressed water. Results obtained at long TE were expressed as ratios of the areas under the Cho, Cr, and NA groups. After confirmation of underlying assumptions such as normality of the distribution of data and sphericity, spectra were compared. using a mixed-design factorial ANOVA.

Results: One-hundred percent compliance was reported both for the Cr supplementation and control groups. Creatine supplemented and placebo group mean spectroscopic results are given in the table below. There were no interactions between groups for either Cr, Cho or NA metabolite areas (at TE=20 ms) or related ratios (at TE=135 ms) indicating that Cr supplementation and placebo groups did not differ significantly in any of the measures ($P > 0.05$).

Figure 1. Volume of interest within the frontal lobe and resultant spectra acquired at short [20ms] and long [135ms] echo times.

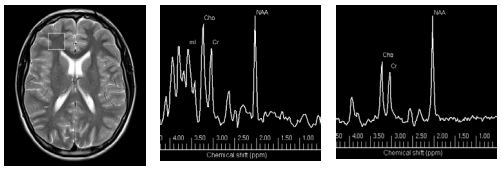

Table 1. Mean spectroscopic metabolite areas and ratios (±1sd).

TE (ms)	Measure (interaction)	Group	Before	After	*P*
20	Cho	Creatine	0.72 ± 0.13	0.74 ± 0.12	0.191
		Placebo	0.60 ± 0.11	0.66 ± 0.08	
20	Cr	Creatine	0.66 ± 0.07	0.73 ± 0.12	0.539
		Placebo	0.66 ± 0.09	0.70 ± 0.04	
20	NA	Creatine	1.22 ± 0.15	1.18 ± 0.18	0.747
		Placebo	1.24 ± 0.16	1.23 ± 0.14	
135	Cho/Cr	Creatine	1.08 ± 0.13	1.03 ± 0.15	0.081
		Placebo	0.90 ± 0.15	0.95 ± 0.12	
135	NA/Cr	Creatine	1.87 ± 0.35	1.68 ± 0.41	0.715
		Placebo	1.89 ± 0.24	1.76 ± 0.18	
135	NA/Cho	Creatine	1.76 ± 0.45	1.64 ± 0.35	0.408
		Placebo	2.14 ± 0.50	1.87 ± 0.35	

Discussion: The findings of this study indicate that, for the given oral supplementation regimen, Cr does not alter the 'MR visible' Cr pool in frontal cerebral white matter of young active sportsmen. This evidence supports the hypothesis that ingested Cr supplementation does not have the potential of altering energy metabolism within the normal human brain at this dosage over this timescale. However, this may contradict research (2) that has focused on a non-sporting population and thus further work is required to elucidate these differences.

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Reference:

1) Romer LM *et al*. Effects of oral creatine supplementation on high intensity, intermittent exercise performance in competitive squash players. Int J Sports Med 2001; 22:546-552.

2) Dechent P *et al*. Increase of total creatine in human brain after oral supplementation of creatine monohydrate. *Am J Physiol* 1999; 277:R698-R704.