Brain creatine depletion in vegetarians? A cross-sectional $^1$H-magnetic resonance spectroscopy ($^1$H-MRS) study

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Abstract

The present cross-sectional study aimed to examine the influence of diet on brain creatine (Cr) content by comparing vegetarians with omnivores. Brain Cr content in the posterior cingulate cortex was assessed by proton magnetic resonance spectroscopy ($^1$H-MRS). Dietary Cr intake was assessed by 3 d food recalls. Vegetarians had lower dietary Cr intake than omnivores (0·03 (SD 0·01) v. 1·34 (SD 0·62) g/d, respectively; $P=0·005$). However, vegetarians and omnivores had comparable brain total Cr content (5·999 (SD 0·811) v. 5·917 (SD 0·665) IU, respectively; $P=0·77$). In conclusion, dietary Cr did not influence brain Cr content in healthy individuals, suggesting that in normal conditions brain is dependent on its own Cr synthesis.

Key words: Brain metabolism; Brain creatine; Central nervous system; Cognition

Creatine (Cr) is endogenously produced (approximately 1 g/d) as well as ingested from diet (approximately 1–5 g/d), mostly via meat intake. Approximately 95 % of total Cr content is localised in skeletal muscle, while smaller amounts can also be found in other excitory tissues, such as the brain.$^{(1)}$

It has been generally accepted that vegetarians have lower tissue Cr content when compared with omnivores. This assumption particularly holds true with regard to skeletal muscle$^{(2)}$. Furthermore, a large body of evidence suggests that vegetarians respond better to Cr supplementation in terms of muscle Cr accretion$^{(2)}$. However, the extent to which dietary Cr may affect Cr content in other tissues is yet unknown.

In the brain, Cr is thought to exert an important energetic role. This notion has been supported by a large body of evidence, including (1) the presence of Cr kinase isoforms in the central nervous system$^{(3)}$, (2) the relationship between brain Cr depletion and mental retardation, autism, speech delay and brain atrophy$^{(4)}$ and (3) the reversal of these symptoms after oral Cr intake$^{(4,5)}$. Recently, it has been demonstrated that orally ingested Cr is able to penetrate the blood–brain barrier, though with some limitations, and improve brain energy metabolism in human subjects$^{(6,7)}$. As a result, it has been suggested that Cr supplementation may alleviate mental fatigue induced by stressor stimulus, such as sleep deprivation combined with vigorous physical activity$^{(8)}$. Additionally, a recent study has demonstrated that in vegetarians, but not in omnivores, Cr supplementation improves memory (as assessed by the word recall test)$^{(9)}$. The latter finding allows speculating that vegetarians may have suboptimal levels of brain Cr, similar to those observed in skeletal muscle.

The aim of the present study was to gather knowledge on the influence of diet on brain Cr content by comparing vegetarians (who consume virtually no Cr from diet) with omnivores.

Materials and methods

In the present cross-sectional study, fourteen healthy vegetarians who had been on a vegetarian diet for 9 (SD 10) years (six women and eight men) were compared with fourteen age- and BMI-matched omnivorous individuals (five women and nine men). No statistical differences between vegetarians and omnivores were detected for any of the demographic variables (Table 1).

The participants were recruited by placing advertisement posters around the researchers’ workplaces as well as in social networking websites. The individuals who volunteered for participation were self-identified as lacto-ovo-vegetarians ($n$ 10), ovo-vegetarians ($n$ 2), vegans ($n$ 2) or omnivores.
Table 1. Characteristics of the participants (Mean values and standard deviations)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vegetarians (n 14)</th>
<th>Omnivores (n 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean 30 ± 5</td>
<td>Mean 30 ± 8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.5 (11.0)</td>
<td>74.2 (14.5)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.71 (0.07)</td>
<td>1.72 (0.09)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.4 (3.0)</td>
<td>24.8 (3.1)</td>
</tr>
<tr>
<td>Schooling (years)</td>
<td>17 (3)</td>
<td>17 (5)</td>
</tr>
</tbody>
</table>

Fig. 1. T1-weighted magnetic resonance (MR) images showing the volume of interest selected for proton MR spectroscopy in the posterior cingulate cortex (total volume = 3*3*3 cm³).

Discussion

The main finding of the present study is that dietary Cr intake does not have any influence on brain Cr content in apparently healthy subjects, as opposed to what is observed in skeletal muscle.

It has been shown previously that oral Cr intake can have beneficial effects on cognitive function in vegetarians rather than in omnivorous individuals(9), suggesting that the former may show some deficit in brain Cr content. However, the present study refutes this hypothesis, reinforcing previous experimental data suggesting that brain Cr content relies primarily on local endogenous synthesis rather than on Cr dietary intake(15). In fact, the key enzymes involved in the two-step Cr synthesis, i.e. arginine:glycine amidotransferase and S-adenosyl-L-methionine:N-quanidinoacetate methyltransferase, are present in astrocytes, neurons and oligodendrocytes, giving the all the main cell types of the brain the potential to synthesise Cr(15,16).

In contrast, brain permeability to Cr is very limited, probably due to the absence of Cr transporter 1 expression in the astrocytes involved in the blood–brain barrier. Together, these observations have led some authors to consider that the brain may show some deficit in brain Cr content. However, the present study refutes this hypothesis, reinforcing previous experimental data suggesting that brain Cr content relies primarily on local endogenous synthesis rather than on Cr dietary intake(15). In fact, the key enzymes involved in the two-step Cr synthesis, i.e. arginine:glycine amidotransferase and S-adenosyl-L-methionine:N-quanidinoacetate methyltransferase, are present in astrocytes, neurons and oligodendrocytes, giving the all the main cell types of the brain the potential to synthesise Cr(15,16).

In apparent contrast to our findings, there is compelling evidence that Cr supplementation can increase brain Cr content and, hence, overcome cognitive impairments (e.g. mental retardation, autism and speech delay) in children with Cr deficiency syndromes(5). Additionally, a few(8,17) but not all(18) studies have revealed a positive effect of Cr...
supplementation on cognition in individuals exposed to highly stressing conditions (e.g. sleep deprivation and exhausting exercise). In light of these data, it is possible to speculate that dietary Cr may be potentially relevant to brain metabolism in 'extreme' conditions where inherent (e.g. X-linked Cr transporter defect) or environmental (e.g. acute mental stressors) factors lead to a Cr depletion that cannot be compensated by endogenous Cr production. Based on the present findings, one can assume that vegetarianism is not a condition that predisposes to brain Cr depletion in the posterior cingulate cortex. However, further studies are needed to determine whether this is the case for other regions of the brain. Additionally, novel investigations must explore the potential differential response to high-dose Cr intake (i.e. Cr supplementation) in vegetarians and omnivores.

In conclusion, dietary Cr intake seemed not to influence brain Cr content in healthy adults, suggesting that in normal conditions, brain is dependent on its own Cr synthesis.

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None of the authors has any conflicts of interest to declare.

References