**Author’s reply: Letter to the Editor: Double-counting due to inadequate statistics leads to false-positive findings in “Effects of creatine supplementation on memory in healthy individuals: a systematic review and meta-analysis of randomized controlled trials”**

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In their letter to the Editor, Eckert and Pascher correctly identified a flawed statistical analysis that warranted correction pertaining to the increased statistical power of our previous meta-analysis on creatine supplementation and memory performance.(1) The inclusion of multiple memory-related outcomes from each study was accompanied with an increased number of same participants (double counting). This could have altered the outcome estimates in the meta-analyses, indeed leading to an increased risk of false-positive findings. To address this, we have now derived the average effect size for studies presenting multiple memory performance outcomes (expressed as composite score) through pooled means and standard deviations for each intervention group.

Following correction, our overall analysis showed that creatine monohydrate does not improve overall memory performance (SMD: 0.19; 95% CI, -0.07 – 0.46, *I2* = 4%; *P* = 0.15) (Figure 1). Subgroup analyses revealed no differences of creatine monohydrate supplementation with low (≤ 5 g/d) (SMD: 0.25; 95% CI, -0.14 – 0.64, *I2* = 0%; *P* = 0.21) or high doses (> 5 g/d) (SMD: 0.17; 95% CI, -0.34 – 0.69, *I2* = 50%; *P* = 0.51) (Figure 2A). However, although young adults (11 – 31 years) did not benefit from creatine monohydrate (SMD: 0.02; 95% CI, -0.27 – 0.31, *I2* = 0%, *P* = 0.90), its effects were prominent in older adults (66 – 76 years) (SMD: 0.80; 95% CI, 0.25 – 1.34, *I2* = 0%, *P* = 0.004) (Figure 2B), which was the main finding of our previous work.(1) Furthermore, no changes were displayed regarding treatment duration (≤ 2 weeks; SMD: 0.16; 95% CI, -0.23 – 0.56, *I2* = 33%, *P* = 0.42) (> 2 weeks; SMD: 0.30, 95% CI, -0.17 – 0.76, *I2* = 0%, *P* = 0.21) (Figure 2C) nor sex (females and males; SMD: 0.18; 95% CI, -0.20 – 0.56, *I2* = 31%, *P* = 0.36) (females; SMD: 0.42; 95% CI, -0.14 – 0.98, *I2* = 0%, *P* = 0.14) (males; SMD: -0.11; 95% CI, -1.01 – 0.79, *P* = 0.81) (Figure 2D). Our sensitivity analyses showed no effects of creatine monohydrate on memory performance in non-encapsulated form (SMD: 0.22; 95% CI, -0.08 – 0.52, *I2* = 16%, *P* = 0.15) (Figure 3A), normal (SMD: 0.29; 95% CI, -0.09 – 0.68, *I2* = 35%, *P* = 0.14) or stressed conditions (SMD: 0.03; 95% CI, -0.46 – 0.52, *I2* = 0%, *P* = 0.91) (Figure 3B), and participants lost to follow up (< 15%) (SMD: 0.28; 95% CI, -0.02 – 0.59, *I2* = 1%, *P* = 0.07) (Figure 3C).

Taken together, the above findings confirm the prominent effect of creatine monohydrate on indices of memory in older adults. It is worth noting however that these results are based on a limited number of participants, hence, future randomized controlled trials are warranted to verify such findings. Finally, we would like to thank the authors for their feedback and hope that our study in combination with the concerns highlighted, will form the basis for future robust research on the topic.

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**Conflicts of interest**

The authors declare no conflict of interest.

**References**

1. Prokopidis K, Giannos P, Triantafyllidis KK *et al.* (2022) Effects of creatine supplementation on memory in healthy individuals: a systematic review and meta-analysis of randomized controlled trials. *Nutr Rev*.

**FIGURES**

**Figure 1.** Effect of creatine monohydrate supplementation on overall memory.

BBCS, Brief Battery of Cognitive Screening; DT, Differentiation Task; RAVLT, Rey Auditory Verbal Learning Test; (R)CBT, Reverse Corsi Block Test; VFDST, Visual Forward Digit Span Test

**Figure 2.** Subgroup analysis of the effect of creatine monohydrate supplementation on overall memory based on dose (A), age (B), duration (C), sex (D).

BBCS, Brief Battery of Cognitive Screening; DT, Differentiation Task; RAVLT, Rey Auditory Verbal Learning Test; (R)CBT, Reverse Corsi Block Test; VFDST, Visual Forward Digit Span Test

**Figure 3.** Sensitivity analysis of the effect of creatine monohydrate supplementation on memory performance based on form of creatine (A), stress status (B) and lost rate during follow-up (C).

BBCS, Brief Battery of Cognitive Screening; DT, Differentiation Task; RAVLT, Rey Auditory Verbal Learning Test; (R)CBT, Reverse Corsi Block Test; VFDST, Visual Forward Digit Span Test