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Letter to the Editor

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Letter to the Editor

Response to Letter by Benson *et al.* on 'Hangover and the Effects of L-Cysteine'

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We are grateful to Benson *et al.* (2021) for their interest in our report on Hangover and the Effects of L-Cysteine (Eriksson *et al.*, 2020). Their first criticism concerned our use of correlations in analyzing the data. We believe that the finding of significant correlations, all in the same direction, does support the hypothesis that L-cysteine alleviates and/or prevents hangover symptoms. Regarding our choice to place statistical results in the Figure legends, we suggest that readers often look more at the Figures than the text, especially when, as in our paper, original data are displayed in the Figures.

Benson *et al.* (2021) suggest that we should have used two-tailed rather than one-tailed tests. However, our starting point was that acetaldehyde is known to cause harmful effects after drinking alcohol and that L-cysteine, widely recognized as binding to acetaldehyde, could be expected to reduce acetaldehyde levels in the body and its harmful effects. Thus, our presumption was that L-cysteine could alleviate and/or prevent the harmful effects of the acetaldehyde, justifying the use of one-tailed tests given that we have a specific prediction about the direction of the difference (i.e. Group A scoring higher than Group B). Benson *et al.* make it clear that they concur with that prediction. We apologize that it was not well formulated in our note on Statistical Methods. The results showed that the impact of L-cysteine on hangover, nausea, headache, stress, anxiety and acetaldehyde is all in the same direction.

Benson *et al.* (2021) ask why we did not use the Bonferroni correction. As previous authors have argued (Rothman, 1990; Perneger, 1998; Armstrong, 2014), Bonferroni corrections have limitations, such as in our study where we used only five different categories (hangover, nausea, headache, stress and anxiety), and all categories differed regarding the number of volunteers and their interconnections with the different hangover symptoms.

Regarding the semi-naturalistic study by Scholey *et al.* (2020) that did not report a protective effect of L-Cysteine, we would make the following comments: Your study included 13 women and 7 men. Women and men are different regarding a number of sex hormones, lack of menstrual cycle and possible intake of oral contraceptives. It would have been good to separately investigate the hangover symptoms in women and men. Also, in order to get the level to the maximum of 1.3 g/kg, the women probably consumed less alcohol—about 25% less because of the water volume and body weight. Combining the results of men and women increases the overall variability. Your participants had a meal before the sessions and apparently did not necessarily consume the maximum dose of 1.3 g/kg of alcohol. This meant that the top alcohol concentration was rather low (0.096%) in comparison to the top concentration (1.3%) in our study (with no meal during the evening). In their Letter, Benson *et al.* (2021) wrote that the L-cysteine dose was 650 mg. In their study (Scholey *et al.* 2020), it is stated that participants were administered a dose in the evening with the final drink and another one upon awakening in the morning. Was the 650 mg divided into these two doses (325 mg/dose)? In any case, the situation is quite different to our study where the participants were administered the doses during the drinking (one per hour) and the study consisted of three sessions (placebo, 600 mg and 1200 mg of L-cysteine). Also, it was not mentioned whether Rapid Recovery tablets were slow release or fast release regarding the L-cysteine. The rationale in our study was to try to neutralize the metabolically generated acetaldehyde at the

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same time as it was formed during alcohol consumption. By giving the L-cysteine only after the evening drinking, acetaldehyde may have already generated the underlying alcohol symptoms, especially concerning nausea.

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