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Impact of AmaTea® Max on physiological measures and gaming performance in active gamers: a placebo-controlled, double-blind, randomized study

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Impact of AMATEA™ on physiological measures and gaming performance in active gamers: a placebo controlled, double-blind, randomized study
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Dear Dr Bloomer,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Jan 04, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: This study of the effects of 270mg of caffeine versus a similarly-caffeinated dietary supplement produced from guayusa (AMATEA) versus placebo concluded that mental and gaming performance as well as vigor, fatigue, and jitteriness scores were improved by AMATEA but not by caffeine. The manuscript is clearly and concisely written, the design is appropriate, and with 49 completed volunteers, the study is adequately powered. Thus, from an experimental standpoint, all is well.

However, the authors draw several conclusions that are not warranted based on the statistical outcomes, and this needs to be corrected prior to publication. Also, the general issue of the failure to find virtually any caffeine effects regardless of whether the caffeine was derived from AMATEA or powder, is worthy of at least some discussion.
1. On page 16, the authors state that gaming performance was impacted by AMATEA™ when measured by kills/match (~12% higher than caffeine; 21% higher than placebo)." In fact, as noted on page 15, there was not a significant condition effect since the p value was only 0.075 and there was no condition-by-time interaction. Thus, neither of the active treatments impacted gaming performance. Statements to the contrary need to either be deleted entirely or appropriately (and heavily) qualified—in both the Discussion section (pages 16 and bottom of 17) and the Conclusions section.
2. On page 16, the statement is made that "Subjects consuming AMATEA™ conveyed fewer reported feelings of jitters than those consuming the same amount of caffeine alone." In fact, the only statistically-significant condition effect for the jittery measure indicated that values were lower for placebo than for caffeine. Thus, there was no difference between AMATEA and caffeine, and indications to the contrary should be deleted anywhere they appear in the manuscript.
3. The second paragraph on page 16 also contains the statement that "Those consuming AMATEA™ reported a less pervasive feeling of fatigue compared to the caffeine group alone." In fact, the only condition effect was due to a difference between caffeine and placebo and not between caffeine and AMATEA. Statements to the contrary should be deleted.
4. A more general issue for consideration is the fact that there were virtually no statistically-significant effects of 270mg of caffeine on a rather lengthy task as well as on some standard mood assessments and a vigilance task. This seems surprising given that the average daily caffeine consumption in the US is supposedly only 135 mg, which would make the active treatment conditions in this study double that amount, and also taken all at once rather than distributed over time as would be the case if the same amount of caffeine were to be consumed in a beverage. At first, I thought this must be a caffeine tolerance issue since as the authors state in the Introduction section "Energy drink consumption is pervasive among gamers and such products often contain caffeine, with assertions that mental fatigue will be attenuated and performance improved via increased alertness and wakefulness… and there is considerable documentation of the nootropic effects of low-dose caffeine, with over 85% of the US population consuming caffeine daily." But when I see that the average consumption of the study sample was only 128mg per day (which in and of itself is surprising), I doubt that

tolerance can be the explanation for the absence of a bolus dose effect. What then explains these results?? At the least, the authors should briefly address this issue in the Discussion section, and they also might consider actually using habitual consumption as a covariate or somehow splitting the sample into high versus low habitual consumers.
5. Finally, I think the authors should explain why they started testing within 5 minutes of the dose administration rather than waiting long enough to ensure that the active treatments hit peak levels in the blood of volunteers. This isn't necessarily a design flaw since a time factor has been included in the experimental design, but it is somewhat of a deviation from typical drug-study procedure.

In summary, this is a nice manuscript that is worthy of publication. However, the results need to be presented in a much more conservative manner, and there needs to be some discussion of the surprising overall absence of caffeine effects. Thank you.

Authors' response

We thank the reviewer for the detailed comments and have addressed these below and within the text. All edits to the manuscript are highlighted in yellow throughout.

Reviewer #1: This study of the effects of 270mg of caffeine versus a similarly-caffeinated dietary supplement produced from guayusa (AMATEA) versus placebo concluded that mental and gaming performance as well as vigor, fatigue, and jitteriness scores were improved by AMATEA but not by caffeine. The manuscript is clearly and concisely written, the design is appropriate, and with 49 completed volunteers, the study is adequately powered. Thus, from an experimental standpoint, all is well.

However, the authors draw several conclusions that are not warranted based on the statistical outcomes, and this needs to be corrected prior to publication. Also, the general issue of the failure to find virtually any caffeine effects regardless of whether the caffeine was derived from AMATEA or powder, is worthy of at least some discussion.

We understand the reviewer's concern and have made edits to the text to better represent the findings, from a statistical perspective.

1. On page 16, the authors state that gaming performance was impacted by AMATEA™ when measured by kills/match (~12% higher than caffeine; 21% higher than placebo)." In fact, as noted on page 15, there was not a significant condition effect since the p value was only 0.075 and there was no condition-by-time interaction. Thus, neither of the active treatments impacted gaming performance. Statements to the contrary need to either be deleted entirely or appropriately (and heavily) qualified—in both the Discussion section (pages 16 and bottom of 17) and the Conclusions section.

This has been done. We reference the p-value of 0.075 as a statistical trend and note this as such. We have amended the statements made throughout. We understand that a trend is not technically viewed as "significant" but we know there are very few gaming studies in the literature and we believe this initial finding is worth mentioning—with the caveat that the finding is a trend and not reaching a value of p<0.05. Thank you.

2. On page 16, the statement is made that "Subjects consuming AMATEA™ conveyed fewer reported feelings of jitters than those consuming the same amount of caffeine alone." In fact, the only statistically-significant condition effect for the jittery measure indicated that values were lower for placebo than for caffeine. Thus, there was no difference between AMATEA and caffeine, and indications to the contrary should be deleted anywhere they appear in the manuscript.

Again, we have made adjustments to the statements based on the statistical analyses. We also analyzed data based on the percentage change from baseline, with no values of significance noted. Thank you.

3. The second paragraph on page 16 also contains the statement that "Those consuming AMATEA™ reported a less pervasive feeling of fatigue compared to the caffeine group alone." In fact, the only condition effect was due to a difference between caffeine and placebo and not between caffeine and AMATEA. Statements to the contrary should be deleted.

We have made adjustments to the statements based on the statistical analyses. Thank you.

4. A more general issue for consideration is the fact that there were virtually no statistically-significant effects of 270mg of caffeine on a rather lengthy task as well as on some standard mood assessments and a vigilance task. This seems surprising given that the average daily caffeine consumption in the US is supposedly only 135 mg, which would make the active treatment conditions in this study double that amount, and also taken all at once rather than distributed over time as would be the case if the same amount of caffeine were to be consumed in a beverage. At first, I thought this must be a caffeine tolerance issue since as the authors state in the Introduction section "Energy drink consumption is pervasive among gamers and such products often contain caffeine, with assertions that mental fatigue will be attenuated and performance improved via increased alertness and wakefulness… and there is considerable documentation of the nootropic effects of low-dose caffeine, with over 85% of the US population consuming caffeine daily." But when I see that the average consumption of the study sample was only 128mg per day (which in and of itself is surprising), I doubt that tolerance can be the explanation for the absence of a bolus dose effect. What then explains these results?? At the least, the authors should briefly address this issue in the Discussion section, and they also might consider actually using habitual consumption as a covariate or somehow splitting the sample into high versus low habitual consumers

This is a valid point and we have added text to the Discussion section. We also pulled out those subjects with greater than 300mg daily caffeine intake, along with those with essentially no daily caffeine intake. When analyzing these different groups, there remain no statistically significant differences in performance (e.g., AX-CPT) or subjective feelings (e.g., such as jitters) between conditions. We were also surprised at these findings. That said, a review of research specific to caffeine and the physiological effects has noted mixed findings with regards to caffeine and cognition.

5. Finally, I think the authors should explain why they started testing within 5 minutes of the

dose administration rather than waiting long enough to ensure that the active treatments hit peak levels in the blood of volunteers. This isn't necessarily a design flaw since a time factor has been included in the experimental design, but it is somewhat of a deviation from typical drug-study procedure.

This is a good point and we considered this when designing the study. The reason for the timing is that subjects were to be tested over an approximate 6-hour period (pre and post tests, along with actual gameplay) and we knew that we would be capturing the peak caffeine concentration likely toward the end of their initial hour of gameplay (which was desired). We did not want to further extend the timeframe of subject participation, as we thought that fatigue would be increased and enthusiasm for participation would wane.

In summary, this is a nice manuscript that is worthy of publication. However, the results need to be presented in a much more conservative manner, and there needs to be some discussion of the surprising overall absence of caffeine effects. Thank you.

2nd Editorial decision
08-Jan-2022

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Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: