

MANUSCRIPT PEER REVIEW: A HELPFUL CHECKLIST FOR STUDENTS AND NOVICE REFEREES

Douglas R. Seals and Hirofumi Tanaka

*Department of Kinesiology and Applied Physiology,
University of Colorado at Boulder, Boulder, Colorado 80309*

The ability to contribute consistent, fundamentally sound critiques is an essential element of the scientific peer review process and an important professional skill for investigators. Despite its importance, many students and junior scientists do not have an adequate working knowledge of how to effectively critique research manuscripts. Part of the problem, in our view, is that novice referees often lack a comprehensive understanding of the basic issues that should be considered in evaluating scientific articles. Specifically, they tend to overemphasize certain limitations (usually methodological), while missing other key points related to the scientific method that should be weighed much more heavily. In our journal club and graduate courses we have been using a “checklist” to help graduate students and postdoctoral fellows critically analyze original research papers. In this article we present these guidelines in the hope that they will serve as a helpful resource for students and other novice reviewers when critiquing scientific manuscripts.

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The ability to develop fundamentally sound, objective critiques of scientific manuscripts is an essential element of the peer review process and, therefore, is an important professional skill for investigators. All physiology journals, including American Physiological Society journals, use some form of peer review. Reviewers evaluate the scientific rationale and significance of the questions/hypotheses, strengths and limitations of the study design and methods, the quality and originality of the data, and the key findings. This process serves to ensure that significant concerns that could impact the important observations and conclusions of the study are resolved before the article reaches the journal readers. Indeed, it has been demonstrated that peer review produces measur-

able and substantial improvements in the quality of manuscripts (1, 7).

In recent years, there has been an ever-increasing emphasis on the peer review system (3, 8, 10). Despite its critical importance, it is well recognized that many beginning scientists do not possess adequate skills for effective appraisal of manuscripts (2, 8, 9). Development of sound critiquing skills is essential to prepare students and other junior investigators for such future editorial tasks.

In a recent survey (6), many novice referees indicated that “some general guidelines as to how to go about the review process would have been helpful.” Many

journal editors recognize this problem and support such training aids as a mechanism to support high-quality reviewing (4, 5). Consistent with this idea, in 1995 Rangachari and Mierson (9) published a brief checklist in *Advances in Physiology Education* to help undergraduate students analyze published scientific articles. Over the past decade we have been refining a more comprehensive checklist aimed at graduate students and postdoctoral fellows. Our checklist is formatted for the purpose of reviewing manuscripts submitted for publication, but it serves as an equally effective guideline for evaluating published papers. Feedback has been positive: students in our journal club and graduate courses perceive this as a very helpful guide.

Our aim here is to present the current working version of our checklist. We have emphasized the important points in a standard IMRAD format: introduction, methods, results, and discussion, followed by some general points of consideration and discussion. It is hoped that these guidelines will serve as a useful resource for students and novice reviewers in developing this challenging but essential professional skill. This should, in turn, result in more high-quality critiques of scientific manuscripts in the future.

IMPORTANT POINTS TO CONSIDER WHEN CRITIQUING SCIENTIFIC ARTICLES

Journal

- Is the topic appropriate for the journal selected? Would another journal be more appropriate?

Comment: When addressing these questions, the stated mission of the journal should be considered along with the interests of the readership. A relatively common example is the case in which a manuscript focusing on a clinical population and/or problem is submitted for publication to a basic science rather than a clinical science journal.

Title

- Does the title accurately reflect the purpose, design, results, and conclusions of the study?

Comment: A case in point would be a cross-sectional study that compared blood pressure in human subjects with low and high dietary sodium intake entitled "Effects of sodium intake on blood pressure in humans." This title could mislead the reader into assuming that the study involved a dietary intervention in which sodium intake was experimentally manipulated. A more precise (and appropriate) title would be "Blood pressure in humans with low and high sodium intake."

Abstract/Summary

- Is this a succinct, clear, and comprehensive summary of the main text of the paper?
- Is the content (data, conclusions, etc.) consistent with that presented in the main text?
- Are data or other key information presented here but not in the main text (or vice versa)?

Introduction

- Does the introduction succinctly state what is known and unknown about the topic?
- Are any important findings from previous studies omitted or misrepresented?

Comment: Unfortunately, either intentionally or by mistake, this occurs rather frequently and, thus, should be monitored carefully.

- Is the functional, biological, and/or clinical significance of the topic established?

Comment: This is important because a key finding can be "new" without being particularly significant. The new information presented should advance the collective knowledge of the issue in question in some obvious manner. The findings must be new (novel) and important.

- Is the specific experimental question, goal, or aim to be addressed stated?
- Are previous experimental observations linked together to establish a formally stated and testable working hypothesis? Does the hypothesis clearly indicate the direction of the postulated effect?

Comment: Some manuscripts will state a purpose to “examine,” “compare,” or “characterize” observations. In most cases, this is not an appropriate substitute for a formally stated working hypothesis and may reflect a scientific investigation that is neither properly focused nor hypothesis driven.

- If previous reports have addressed the same topic: 1) are their strengths and limitations described such that the need for further study is established? and 2) is it clear how the experimental approach to be used in the present study is likely to yield more definitive or unique insight than these previous studies?

Comment: Occasionally the introduction of a manuscript will describe the findings of previous studies without it being clear how they collectively establish the need for additional investigation to answer the question. More commonly, the new study is proposed in a manner in which it appears to be similar to previous investigations on the same topic (i.e., “more of the same”) rather than a new, more effective approach that could result in the resolution of currently controversial and/or equivocal findings.

Methods

- Are the subjects adequately described (i.e., do you know everything you need to for proper interpretation of the results)?

Comment: See below regarding confounding factors.

- Is the subject population appropriate for the question posed?

Comment: An investigation designed to determine whether regular exercise can lower plasma cholesterol levels, but consisting strictly of subjects who are lean, physically active vegetarians (most of whom likely have low cholesterol levels at baseline) has little chance of showing such an effect, and the results would have little meaning for society as a whole.

- Is the number of subjects sufficiently large to provide the necessary statistical power to show a difference if it is really present (i.e., minimize the likelihood of producing a type II error)?

- Will the subject population allow extensive or rather limited generalizability?

Comment: A well-controlled study showing no influence of a particular intervention on a physiological response in normally functioning, healthy young adults may have little relevance to older adults or patients with disease in whom a significant effect may occur.

- Was the assignment of subjects to conditions randomized?
- Are ethical issues such as informed consent and institutional review board approval described?
- Are proper control groups and/or conditions included?

Comment: A physiological function (e.g., resting blood pressure) may normally change with repeated measurement (familiarization effect) and, thus, would require the appropriate time controls for proper interpretation.

- Does the experimental design allow the hypothesis to be tested in a rigorous scientific manner? Is there a better experimental approach that could have been employed?

Comment: If a longitudinal design is optimal, does the cross-sectional comparison used instead provide sufficiently interpretable new and important information?

- Do the experimental design and the protocols employed control for all potential confounding factors? Stated another way, does the experimental approach effectively isolate the mechanism or factor of interest?

Comment: One approach is to list all of the factors (subject characteristics, ambient conditions, etc.) that are known or suspected to influence the key outcome variable(s) and determine whether those factors were properly controlled or at least accounted for. If not, ask yourself whether that factor could contribute to an alternative explanation of the results (i.e., other than that suggested by the authors).

- Was each methodology described in sufficient detail for others to repeat the study? If not, do the authors provide a proper (i.e., peer reviewed) reference that would provide such details?

Comment: Either details need to be provided or a reference describing those details needs to be cited. Also, if the procedure previously has passed peer review in a prestigious scientific journal, you may reasonably have more confidence in the appropriateness of its use.

- Are the measurement techniques used sufficiently reliable, precise, and valid?
- Is the rationale for making each measurement either obvious or explained?

Comment: It should be clear as to how each measurement described was necessary (required) for the proper interpretation of the experimental results as they pertain to testing the working hypothesis(es).

- Have the data been analyzed in the most appropriate manner? Were the investigators properly “blinded” in the analysis to eliminate possible bias?
- Are the details as to how data were derived (calculated) adequately explained so that they can be confirmed by the reviewer and reproduced by future investigators?
- Is it clear how the data will be interpreted to either support or refute the hypotheses?

Comment: If not, there likely is a fundamental problem with the study design.

- Are the statistical techniques used appropriate for the experimental design?
- Are any critical assumptions of the statistical techniques (e.g., independence, homogeneity, normality) violated?
- Are the alpha-levels (or the significance level) used to determine statistical significance clearly stated?

Results

- Are the data reported in a clear, concise, and well-organized manner?
- Where necessary, are standard deviations or standard errors reported for each variable? Is there exces-

sive variability in one or more of the measurements for a particular condition compared with the others?

Comment: The variability associated with a mean value may explain the lack of statistically significant differences, indicate possible errors or poor reliability in certain measurements, and provide important insight into other aspects related to the results.

- Are data presented on any measurement that was not described in the Methods? Alternatively, are the data on all measurements described in the Methods presented?
- Have the data been presented in the appropriate units (e.g., absolute unit changes vs. percentage changes) or properly adjusted statistically (e.g., when there are differences in the baseline values of variables that could confound interpretation of the results)?
- Have tables, figures, and text (the 3 tools used to present data) been used effectively?

Comment: When possible, most investigators use figures to emphasize their most important results.

- Are all the figures and tables needed?

Comment: Perhaps a bar graph figure is being used to show a few values (not on key outcome variables) that could be more economically presented in the text of the Results section or as part of an existing table.

- Are the tables and figures properly labeled with the correct units?
- Is the scaling of the figures appropriate and unbiased?

Comment: Small, physiologically insignificant mean differences can appear much larger when an inappropriately small scale is used; this can mislead the reader. Alternatively, important mean differences can be underemphasized if inappropriately large scaling is employed.

- Are the labels on both axes sufficiently large to be readable after the reduction in size for publication?
- Are any data presented more than once in the same form (e.g., absolute unit values for glucose uptake are shown in the text or a table and also in a figure)?

- Do the data seem reasonable from a physiological perspective?

Comment: It is important to view the values or responses in the context of the known physiological baseline levels, reserve range, and maximal capacity (in addition to the stimulus intensity, etc.) to help ensure that the data are appropriate and believable.

- How do the group differences or responses shown compare with the measurement variability?

Comment: A 5% difference in mean group responses for an outcome variable that is associated with a 10% measurement error/variability would need to be interpreted with extreme caution.

Discussion

- Are the major new findings of the study clearly described and properly emphasized?

Comment: The authors should be clear and up front as to their important new findings.

- Are the key conclusions adequately supported by the experimental data?

Comment: This is critical. You must make sure that the conclusions of the study are consistent with the results.

- Is there any other way to interpret and/or explain the data other than that suggested by the authors?

Comment: One of your primary responsibilities as a reviewer is to identify and develop arguments in support of alternative explanations to the author's conclusions. An example would be a manuscript that concludes that primary human aging causes left ventricular hypertrophy on the basis of a cross-sectional comparison of groups of young and older adults. However, you may determine that the older subjects also were hypertensive, and that hypertension is independently associated with left ventricular hypertrophy. Thus, an alternative explanation would be that it was the high blood pressure, not the

age, of the older subjects that caused their greater left ventricular wall thickness.

- Is the significance of the present results described? Is it clear how the findings extend previous knowledge in a meaningful way?

Comment: Some physiology journals require authors to comment on the significance of their findings. You should consider this requirement regardless of mandatory journal guidelines.

- Are important experimental observations from previous reports described in the context of the present results?

Comment: Knowledge on the topic can be optimally advanced only if previous findings and the current results are effectively integrated to establish a new understanding of how the system in question works (or at least how it may work).

- Do the authors support their statements with appropriate references? • Do the authors discuss their data in a manner that provides insight beyond that presented in previous sections?

Comment: It is not sufficient to simply restate the experimental questions and key results. It is the obligation of the authors to discuss their findings in a way that extends our current understanding of the physiological regulation or adaptations in question.

- Are the unique aspects and other experimental strengths of the study properly highlighted?

Comment: It is important to emphasize how the experimental design, methods, and other features of the study are unique and, as a result, have produced novel findings.

- Are the important experimental limitations of the study described so that the reader will be able to interpret the findings appropriately?

Comment: It is very important that the authors discuss such limitations in a good faith manner that properly informs the reader of considerations that

could affect how they (the reader) view the key conclusions.

- Do the authors make suggestions as to how the results of their study need to be extended in the future to learn more about the issue in question?

General

- Is the manuscript concise (are there unnecessary sections that should be shortened or eliminated)?

Comment: If you request that the manuscript be shortened, be specific as to those sections or paragraphs that you deem to be unnecessary or overly long. It is frustrating for authors (and poor reviewing in our opinion) to receive a vague comment that a paper is too long and should be shortened without any justification or guidance.

- Was the paper well written, properly organized, and easy to follow?
- Was the information presented in an open-minded and objective manner?

Comment: Remember that you are the key “consumer advocate” in this process. It is your responsibility to ensure that issues are discussed in a fair and unbiased way that best informs and generally serves the interests of the reader.

- Is there a significant conflict of financial or scientific interest?

Comment: For example, was the study supported by industry or some organization that may have directly or indirectly influenced the manner in which the results are presented, interpreted, or discussed?

- Helpful hint: Focus on aspects of the study and/or paper that fundamentally affect the key conclusions. *This is the most common mistake made by novice reviewers in our experience.* If your criticism does not alter the primary conclusions of the study, it probably is not worth emphasizing, particularly in the “major comments and/or recommendations” section of your review (see below). Instead, mention those points only as “minor” comments.

PERSPECTIVES

In considering your responses to the above points, how would you describe the overall quality of the study and manuscript? How could they be improved? Your judgments should be based on an objective assessment of the strengths and weaknesses of the paper rather than on personal opinions and/or biases.

You must now integrate your observations, opinions, and ideas on the manuscript to construct an effective critique. Each journal or society has its own distinct reviewer forms and instructions. However, we believe that most good manuscript reviews adhere to certain common guidelines. The critique needs to be written clearly and succinctly, and it must above all be *informative* for both the authors and the editor. The review should comment on both the strengths and the weaknesses of the paper, although the latter usually requires more space because the referee needs to explain his or her concerns and how those concerns can be resolved. It is important that the reviewer indicates what the problems are and exactly how they could or should be addressed. It is very frustrating for authors to read reviewer comments that contain vague and/or generic criticisms without clear recommendations for specific revision action items in the form of additional experiments that need to be performed and/or changes to the manuscript. A systematic, well-organized review will be appreciated and will facilitate the manuscript revision (or, if rejected, the resubmission) effort. As mentioned above, it is important for reviewers to organize their comments in a way that distinguishes between the major concerns on which the acceptability of the manuscript depends and the necessary “housekeeping” chores associated with the revision process (correcting typographical errors, minor wording changes, adding informational details, etc.). The latter are indeed essential (they should not be considered “optional”), but author and editor both benefit from a clear delineation of the “major” and “minor” concerns of the reviewer.

One of the reviewer forms that you will receive from the editorial office of the journal will ask you to make a decision on the acceptability of the manuscript for publication in its present form. From a procedural standpoint, such a decision can be made before or after developing your critique. In some cases, the

issue will be obvious: you will know after reading the paper that it should be accepted or rejected. However, frequently there is some question as to whether a major revision or a rejection should be recommended. In such cases, we suggest that you develop your written critique *before* deciding on your recommendation. In our experience, often an objective reviewer will have a clearer position on this point after undergoing the intellectual process involved in developing a thorough written analysis of the paper.

Finally, how do you decide whether, considering all of the above issues, a particular manuscript is worthy of recommendation for publication? As you might suspect, there is no definitive or easy-to-use procedure to follow. In the end, the process is subjective—you must decide. However, in our view, reviewers should focus on several key points described in the checklist including

- The appropriateness of the manuscript for the journal; if not appropriate, the paper cannot be acceptable regardless of its scientific merit.
- Is the experimental question *significant*? If not, the other issues are not relevant.
- Is a clear and testable hypothesis presented?
- Is the overall experimental approach (including subjects, study design, key methods, and data analysis) valid?
- Are the results properly presented and believable?
- Are the conclusions reasonable on the basis of the results obtained (i.e., have the experimental data been properly interpreted)?
- Are the major findings both novel and important (i.e., has sufficient new knowledge been gained)?

This is not to suggest that the other checklist items are not important, only that certain considerations need to be weighed more heavily than others when determining the acceptability of a manuscript for publication. With experience, you may decide that some of the above issues are not critical and/or that others from the checklist (or other sources) need to be added. That is a natural step in the learning process for developing this (or any other) professional skill.

In summary, this checklist is meant to be a *general guide* to students and other novice reviewers for the effective evaluation of original scientific manuscripts. As these individuals become more experienced most, if not all, of these points will become intuitive, and individual approaches will be established. The hope here is that our checklist will, in the meantime, provide some helpful structure in what can be a daunting challenge for the inexperienced.

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Address for reprint requests and other correspondence: D. R. Seals, Dept. of Kinesiology and Applied Physiology, Campus Box 354, Univ. of Colorado at Boulder, Boulder, CO 80309-0354 (E-mail: seals@colorado.edu).

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