The effects of phylogeny, habitat and host characteristics on the thermal sensitivity of helminth development

Jessica Ann Phillips, Juan S. Vargas Soto, Samraat Pawar, Janet Koprivnikar, Daniel P. Benesh and Péter K. Molnár

Review timeline
Original submission: 23 August 2021
Revised submission: 20 November 2021
Final acceptance: 4 January 2022

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

Review History
RSPB-2021-1878.R0 (Original submission)

Review form: Reviewer 1

Recommendation
Accept with minor revision (please list in comments)

Scientific importance: Is the manuscript an original and important contribution to its field?
Excellent

General interest: Is the paper of sufficient general interest?
Good

Quality of the paper: Is the overall quality of the paper suitable?
Excellent

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No
Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.

No

It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.

Is it accessible?
Yes

Is it clear?
Yes

Is it adequate?
Yes

Do you have any ethical concerns with this paper?

No

Comments to the Author

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I only have a few minor suggestions for the authors to consider:

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Line 292: I think this sentence should start ‘The fact that phylogeny…’

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Table 1. Is there a graphical way to represent this information? Maybe consider displaying the estimates of each term in the model. Further, showing the direction of the effects of the covariates would be useful.
Review form: Reviewer 2

Recommendation
Accept with minor revision (please list in comments)

Scientific importance: Is the manuscript an original and important contribution to its field?
Excellent

General interest: Is the paper of sufficient general interest?
Excellent

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Good

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
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Secondly, the authors conclude that “phylogenetic structure was key for explaining the variation in thermal sensitivity in our dataset” (L267). Was there any overall difference between nematodes, trematodes, cestodes or acanthocephalans? As it looks in the phylogenetic structure in Figure 2, there seems to be a large clade with a mix of high (red) and low (blue) AEs (nematodes?), a mid-sized clade with predominantly low (blue) AEs (platyhelminths?), and a small clade with predominantly mid-high (red) AEs (acanthocephalans?).

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L57: Please add a comma after “reference temperature”

L101-102: “We thus focus our analyses on the thermal sensitivity of developmental processes from here on” AE could be mentioned here as well.

L112-143: These are all important factors that might determine the parasites’ temperature sensitivity. Additional factors that could be tested in future analyses could include ‘size of the parasite stage’, ‘host specificity’, ‘type of parasite stage’ (e.g., active transmission stage, active reproduction stage, passive waiting stage etc.), or a further distinction of the aquatic habitat type into ‘freshwater’ vs. ‘marine’. I am not suggesting to include these in the current manuscript but they could be used in future assessments.

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L306-307: “despite the greater temperature fluctuations experienced in terrestrial environments” See my comment regarding intertidal fluctuations.

L314: “Perhaps it is more beneficial to be able to react quickly to the onset of short growing seasons” …especially since transmission windows can be expected to be shorter in cold regions.
Dear Ms Phillips:

Your manuscript has now been peer reviewed and the reviews have been assessed by an Associate Editor. The reviewers’ comments (not including confidential comments to the Editor) and the comments from the Associate Editor are included at the end of this email for your reference. As you will see, the reviewers have raised some concerns with your manuscript and we would like to invite you to revise your manuscript to address them.

We do not allow multiple rounds of revision so we urge you to make every effort to fully address all of the comments at this stage. If deemed necessary by the Associate Editor, your manuscript will be sent back to one or more of the original reviewers for assessment. If the original reviewers are not available we may invite new reviewers. Please note that we cannot guarantee eventual acceptance of your manuscript at this stage.

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When submitting your revision please upload a file under "Response to Referees" - in the "File Upload" section. This should document, point by point, how you have responded to the reviewers’ and Editors’ comments, and the adjustments you have made to the manuscript. We require a copy of the manuscript with revisions made since the previous version marked as ‘tracked changes’ to be included in the ‘response to referees’ document.

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If your study uses animals please include details in the methods section of any approval and licences given to carry out the study and include full details of how animal welfare standards were ensured. Field studies should be conducted in accordance with local legislation; please include details of the appropriate permission and licences that you obtained to carry out the field work.

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It is a condition of publication that you make available the data and research materials supporting the results in the article. Please see our Data Sharing Policies (https://royalsociety.org/journals/authors/author-guidelines/#data). Datasets should be deposited in an appropriate publicly available repository and details of the associated accession number, link or DOI to the datasets must be included in the Data Accessibility section of the
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Online supplementary material will also carry the title and description provided during submission, so please ensure these are accurate and informative. Note that the Royal Society will not edit or typeset supplementary material and it will be hosted as provided. Please ensure that the supplementary material includes the paper details (authors, title, journal name, article DOI). Your article DOI will be 10.1098/rspb.[paper ID in form xxxx.xxxx e.g. 10.1098/rspb.2016.0049].

Please submit a copy of your revised paper within three weeks. If we do not hear from you within this time your manuscript will be rejected. If you are unable to meet this deadline please let us know as soon as possible, as we may be able to grant a short extension.

Thank you for submitting your manuscript to Proceedings B; we look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Best wishes,
Professor Hans Heesterbeek
mailto: proceedingsb@royalsociety.org

Associate Editor
Board Member: 1
Comments to Author:
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Referee: 1
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Author's Response to Decision Letter for (RSPB-2021-1878.R0)

See Appendix A.

RSPB-2021-1878.R1 (Revision)

Review form: Reviewer 1

Recommendation
Accept as is

Scientific importance: Is the manuscript an original and important contribution to its field?
Excellent

General interest: Is the paper of sufficient general interest?
Good

Quality of the paper: Is the overall quality of the paper suitable?
Excellent

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No

Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.
No

It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.

Is it accessible?
Yes

Is it clear?
Yes

Is it adequate?
Yes

Do you have any ethical concerns with this paper?
No

Comments to the Author
The authors have addressed the comments thoroughly. I have no further suggestions and believe this work will be important to the field.
Dear Ms Phillips

I am pleased to inform you that your manuscript entitled "The effects of phylogeny, habitat, and host characteristics on the thermal sensitivity of helminth development" has been accepted for publication in Proceedings B.

You can expect to receive a proof of your article from our Production office in due course, please check your spam filter if you do not receive it. PLEASE NOTE: you will be given the exact page length of your paper which may be different from the estimation from Editorial and you may be asked to reduce your paper if it goes over the 10 page limit.

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Thank you for your fine contribution. On behalf of the Editors of the Proceedings B, we look forward to your continued contributions to the Journal.

Sincerely,
Professor Hans Heesterbeek
Editor, Proceedings B
mailto: proceedingsb@royalsociety.org
Associate Editor:
Board Member: 1
Comments to Author:
Thank you for your careful attention to the last round of revisions and for your thoughtful responses to reviewers. I am now satisfied that all the issues raised during peer review have been addressed. Congratulations on a lovely paper!

Board Member: 2
Comments to Author:
(There are no comments.)
Appendix A

Dear Professor Heesterbeek,

We are pleased to have the opportunity to submit a revised version of our manuscript, “The effects of phylogeny, habitat, and host characteristics on the thermal sensitivity of helminth development” for publication in the *Proceedings of the Royal Society of London Series B* (RSPB-2021-1878). None of the material presented in this paper is published elsewhere or is under consideration for publication elsewhere.

Below, we offer responses (see italicized font) to the suggestions and concerns of the Associate Editor and Reviewers on a point-by-point basis (note that line numbers refer to the revised manuscript with ‘simple markup’ unless otherwise indicated). Thank you again for your consideration of this manuscript.

Sincerely,

Jessica Ann Phillips, Juan S. Vargas Soto, Samraat Pawar, Janet Koprivnikar, Daniel P. Benesh, Péter K. Molnár

Associate Editor
Board Member: 1

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1. REVISE INTRO - Please bring the intro into alignment with the discussion by presenting the concept of AE comprehensively in the introduction section, as suggested by Reviewer 2.

*We have revised the Introduction as suggested (see Lines 50-67) and now provide more information regarding AEs.*

2. QUANTITATIVE COMPARISON OF PARASITE CLADES - Please provide a quantitative comparison of AE among the major parasite clades (e.g., cestodes, trematodes, etc) as requested by Reviewer 2. This can be written in the results or presented as a table/figure at your discretion.

*Please see our response to Reviewer 2 below. We have added a figure to the supplement that illustrates the negligible effect of phylum relative to family when considering comparisons of AE among the helminth taxa.*

3. HOST PHYLOGENY AND BODY SIZE - Please consider Reviewer 1’s suggestion about considering the effects of host phylogeny and body size on parasite AE. You may choose to include these variables in statistical models but, if you do not, please at least address the issue in the discussion.

*Please see our response to Reviewer 1 below. Specifically, we note that the addition of host body size and phylogeny would be challenging because the vast majority of helminth parasites have complex, multi-
host life cycles. As such, it would be necessary to decide which host(s) were relevant in this context (e.g. first or second intermediate hosts or definitive hosts). In addition, a substantial number of activation energy estimates in our analysis are for stages outside of a host, and choosing the host for a stage that occurs either before or after the free-living stage would be an arbitrary decision. It is thus not evident how one might incorporate a single appropriate value related to either host body size or phylogeny for each helminth species. In addition, host phylogeny is already encompassed by some of our covariates, such as the use of animal or plant hosts or aquatic vs. terrestrial life cycles.

We now address this in the Discussion on lines 353-356: “We did not include host phylogeny or body size in this analysis because many helminths have complex life cycles within multi-host systems, and most of our data are restricted to the free-living life stages of parasites. This reflects the difficulty of experimentally measuring traits of helminth parasites across multiple life stages, and especially when they are within hosts.”

Reviewer(s)’ Comments to Author:

Referee: 1

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Thank you!

I only have a few minor suggestions for the authors to consider:

1. I wonder if conducting a comparative analysis of temperature dependences with the addition of host phylogeny is worth considering. It seems like both parasite and host phylogeny would be important and can drive some macroecological patterns (e.g., Harnos et al., 2016’ Size matters for lice on birds: Coevolutionary allometry of host and parasite body size’ Evolution). Thinking about this further, it could be problematic for multi host lifecycles, so I am unsure what host in the lifecycle is the most appropriate to model.

We agree that host phylogeny can be important when investigating certain macroecological patterns, specifically when considering influences of parasitism on hosts. However, our analyses are focused on explaining patterns of AE in parasites, rather than their hosts, and many host traits, including phylogeny, are comparatively less relevant in this context, such as for free-living parasite propagule stages. Some host traits may have an influence on parasite AEs, for example, via the temperature sensitivity of the survival of ectotherm intermediate hosts and the resultant time window that is available for parasite development. However, accounting for such effects through host phylogeny is not possible given the
currently available data, both because related parasites tend to use related hosts (thus confounding parasite and host phylogeny) and because many helminths have complex life cycles, but thermal data only exists for one parasite life stage and often only the free-living ones, as the Reviewer also mentions. Having said that, our analyses do account implicitly for some potential variation through host phylogeny through many of our fixed effects: namely use of plants or animals as hosts, and considering terrestrial vs. aquatic life cycles.

*We have now addressed this in the Discussion on lines 353-356.*

2. Within host groups (e.g., ectotherms), I suspect host body size could be an important covariate in the models presented here. The idea being bigger hosts can provide some sort of thermal inertia for parasites (similar to the ideas in Bergmann’s Rule).

*As mentioned in our preceding response, there is no obvious way to choose which host to focus upon for free-living parasite stages, which encompass a large portion of our dataset. For example, there is no host size for egg development, and selecting a host for this stage would be an arbitrary decision. It isn’t evident how to appropriately calculate or include host body size in these cases to obtain a single measure for each helminth species.*

*We have now addressed this in the Discussion on lines 353-356.*

Line 292: I think this sentence should start ‘The fact that phylogeny...’

*We have modified this sentence to start with “The fact that phylogeny...” on line 294.*

Lines 313-317: This part of the discussion makes me wonder if temperature seasonality (coefficient of variation of temp) would be a useful covariate in the model.

*We did not include the coefficient of temperature variation in our models, but we did include three variables likely correlated with temperature fluctuations: the range in monthly temperature means (Fig. 3b), latitude (Fig. 3c), and habitat (Fig. 3d). AE was not strongly correlated with the first two, but AE did tend to be higher in terrestrial vs aquatic parasites (lines 243-244). Testing whether this reflects adaptation to temperature variability, such as through finer measurements of temperature across seasons, could be an interesting avenue for future research, which we discuss from lines 313-320.*

Table 1. Is there a graphical way to represent this information? Maybe consider displaying the estimates of each term in the model. Further, showing the direction of the effects of the covariates would be useful.

*The goal of Table 1 is to present the model-building approach and summarize model fits, whereas the effect sizes and directions for many model terms are plotted in Figures 3 and 4, and numerous effect sizes, such as slopes, are stated in the results. Thus, while we agree that graphical representations can be helpful, we think that doing so, in this case, would introduce some redundancy.*
Comments to the Author(s)

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Thank you for this suggestion. We have revised the Introduction to clarify and provide additional information regarding the meaning and interpretation of AE (see Lines 50-67).

Secondly, the authors conclude that “phylogenetic structure was key for explaining the variation in thermal sensitivity in our dataset” (L267). Was there any overall difference between nematodes, trematodes, cestodes or acanthocephalans? As it looks in the phylogenetic structure in Figure 2, there seems to be a large clade with a mix of high (red) and low (blue) AEs (nematodes?), a mid-sized clade with predominantly low (blue) AEs (platyhelminths?), and a small clade with predominantly mid-high (red) AEs (acanthocephalans?).

This is a fair question. Phylogenetic structure can arise anywhere in the tree (i.e. near the tips or near the root), and although Figure 2 gives a sense of where there are shifts in activation energy (AE), it can still be hard to compare clades, like nematodes vs cestodes. Here is a box plot comparing the three helminth phyla in our dataset:
As the reviewer suggests, it looks like Platyhelminthes have lower AE than nematodes, on average. However, we believe it would be premature to conclude that helminth phyla differ in temperature sensitivity because these differences are at least partly driven by some overrepresented taxa. For instance, the median AE for Platyhelminthes is lower because one large taxon, tapeworms in the family Hymenolepidae (58% of the platyhelminth thermal performance curves), happen to have low AE. Other platyhelminth families had AEs closer to the overall median (Fig. S2 in the original submission, now Fig. S3).

The family-level means in Fig. S3 were estimated with a model including all taxonomic levels (phyla to species), i.e. the taxonomic version of the phylogenetic ‘base’ model in Table 1. We had noted in the supplement that family was the most important taxonomic level in this model. A complementary way to examine where differences in temperature sensitivity arise is to fit a series of nested models. Specifically, we added taxonomic levels to the model from the root to the tips, i.e. start with a model with just phylum, then add class, then order, etc. A given taxonomic level should improve the model if AE differs between groups and is consistent within them. At each step, we quantified the variation explained by taxonomy. The largest jumps in explanatory power were observed when we added order and family to the model; adding order increased the variation explained from 17 to 46%, and family increased it further to 59%. This is summarized in the following figure, which is now Figure S2 in the supplement:
Note that although the phylum-only model explains little variation in AE, there are wide credible intervals around the phylum-level random effect. Thus, the available data suggest that helminth phyla do not differ in temperature sensitivity overall, but given the limited number of species studied to date, further sampling is needed to strengthen this conclusion. We hope that our analysis, by identifying which helminth clades have and have not been studied, will stimulate such research.

In sum, we made the following changes to better illustrate where there are differences in temperature sensitivity: (i) we added phyla labels to Fig. 2 (e.g., “Nematoda” on the branch leading to nematodes), (ii) we noted in the results section that differences were mainly among orders and families (line 233-234), and (iii) we added to the supplement the analysis in which taxonomic levels were added sequentially, highlighting orders and families as most explanatory (see section 1.3 in supplement S1).

Furthermore, the following minor comments should also be considered by the authors:

L18: “Helminth parasites are part of almost every ecosystem, with an estimated 1-2 billion people infected at any time.” I find this sentence a bit misleading. Although helminth parasites are indeed very diverse and are present in nearly every ecosystem, only very few taxa in this group are actually infecting humans. Likewise, L35 could be changed to “Some helminth species also take a heavy toll on human health [...]”

We have modified the sentence in line 18 to “Helminth parasites are part of almost every ecosystem, with more than 300,000 species worldwide.” We also modified the sentence in lines 35-36 to “Some helminth species also take a heavy toll on human health, such as schistosomiasis or ascariasis.” as the reviewer suggested.

L57: Pleases add a comma after “reference temperature”
We have now added this comma on line 58.
L101-102: “We thus focus our analyses on the thermal sensitivity of developmental processes from here on” AE could be mentioned here as well.

*We have revised this sentence to “We thus focus our analyses on the activation energies of developmental processes from here on.” on lines 104-105.*

L112-143: These are all important factors that might determine the parasites’ temperature sensitivity. Additional factors that could be tested in future analyses could include ‘size of the parasite stage’, ‘host specificity’, ‘type of parasite stage’ (e.g., active transmission stage, active reproduction stage, passive waiting stage etc.), or a further distinction of the aquatic habitat type into ‘freshwater’ vs. ‘marine’. I am not suggesting to include these in the current manuscript but they could be used in future assessments.

*We now note in the Discussion (lines 356-360) that such potential influences should be considered in future investigations.*

L194: “aquatic habitats could buffer temperature fluctuations” While this is certainly true, it should be noted that many marine organisms (and their parasites) in coastal zones regularly experience dramatic temperature shifts during the tidal cycle (e.g., in small rock pools, or when falling completely dry during low tide).

*This sentence gave the rationale for testing a latitude by habitat interaction. Specifically, seasonal changes in temperature, approximated by latitude, may differ in terrestrial and aquatic habitats and thus shape AE. We have modified this sentence to clarify that this term relates to seasonal temperature fluctuations (lines 193-195). On a daily time scale, though, some aquatic habitats, like tide pools, can experience pronounced temperature swings. We have acknowledged this in the Discussion (line 308-309 and see comment below).*

L215: What does ‘eV’ stand for?

*It stands for electron volts. We have now clarified this in the text on lines 217-218:” The median AE was 0.67 electron volts (eV)...”*

L248: insert space after “prokaryotes”

*Done (line 251).*

L249-251: “meaningful thermal performance data exist for less than 0.1% of the estimated hundreds of thousands of extant helminth species” Moreover, the available data seems skewed towards certain groups of parasites, since the current dataset consists largely of thermal performance values from nematodes, despite trematodes being estimated to make up the largest part of helminth diversity (see [54] Carlson 2020)
We agree that such bias is a problem, and this is noted on line 336: “Our study is limited by the species that have been studied...” We have also added a sentence on lines 348-349: “Nematodes, for example, are overrepresented in our datasets, despite trematodes estimated to represent the largest part of helminth diversity (54).”

L306-307: “despite the greater temperature fluctuations experienced in terrestrial environments” See my comment regarding intertidal fluctuations.

In general, we believe it is a fair assumption that air and soil heat up and cool down faster than water, so terrestrial habitats should, on average, exhibit more temperature variability than aquatic ones. Nonetheless, the reviewer is correct that some aquatic habitats like intertidal and ephemeral ponds are also characterized by large temperature swings. We have revised the sentence to acknowledge this (line 307-309): “Furthermore, AE was higher in terrestrial than in aquatic helminths, despite presumably greater temperature fluctuations in terrestrial environments (though some aquatic habitats, such as tide pools, may also exhibit high temperature variability).”

L314: “Perhaps it is more beneficial to be able to react quickly to the onset of short growing seasons “...especially since transmission windows can be expected to be shorter in cold regions.

We have revised this sentence to “Perhaps it is more beneficial to be able to react quickly to the onset of the shorter growing seasons found in colder regions (high AEs), than to be able to buffer large temperature fluctuations during the growing season with low AEs.” on lines 316-319.