

# Adipocyte function and the development of cardiometabolic disease

Maude Giroud, Henrika Jodeleit, Kacey June Prentice, and Alexander Bartelt  
DOI: 10.1113/JP281979

*Corresponding author(s): Alexander Bartelt (alexander.bartelt@med.uni-muenchen.de)*

*The referees have opted to remain anonymous.*

---

|                         |                     |             |
|-------------------------|---------------------|-------------|
| <b>Review Timeline:</b> | Submission Date:    | 02-Jun-2021 |
|                         | Editorial Decision: | 23-Jul-2021 |
|                         | Revision Received:  | 11-Aug-2021 |
|                         | Editorial Decision: | 24-Aug-2021 |
|                         | Revision Received:  | 25-Aug-2021 |
|                         | Accepted:           | 31-Aug-2021 |

---

*Senior Editor: Ian Forsythe*

*Reviewing Editor: Julie Chan*

## Transaction Report:

(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. Depending on transfer agreements, referee reports obtained elsewhere may or may not be included in this compilation. Referee reports are anonymous unless the Referee chooses to sign their reports.)

Dear Dr Bartelt,

Re: JP-SR-2021-281979 "Adipose tissue browning and cardiometabolic health" by Maude Giroud, Henrika Jodeleit, Kacey June Prentice, and Alexander Bartelt

Thank you for submitting your invited Symposium Review to The Journal of Physiology. It has been assessed by a Reviewing Editor and by 1 expert referee and I am pleased to tell you that it is considered to be acceptable for publication following satisfactory revision.

Please advise your co-authors of this decision as soon as possible.

The reports are copied at the end of this email. Please address all of the points and incorporate all requested revisions, or explain in your Response to Referees why a change has not been made.

**NEW POLICY:** In order to improve the transparency of its peer review process The Journal of Physiology publishes online as supporting information the peer review history of all articles accepted for publication. Readers will have access to decision letters, including all Editors' comments and referee reports, for each version of the manuscript and any author responses to peer review comments. Referees can decide whether or not they wish to be named on the peer review history document.

I hope you will find the comments helpful and have no difficulty in revising your manuscript within 4 weeks.

Your revised manuscript should be submitted online using the links in Author Tasks Link Not Available. This link is to the Corresponding Author's own account, if this will cause any problems when submitting the revised version please contact us.

The image files from the previous version are retained on the system. Please ensure you replace or remove any files that have been revised. Your revised submission should include:

- A Word file of the complete text (including figure legends any Tables);
- An Abstract Figure (with legend in the Article file)
- Each figure as a separate, high quality, file;
- A full Response to Referees;
- A copy of the manuscript with the changes highlighted.
- Author profile. A short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more.

You may also upload:

- A 'Cover Art' file for consideration as the Issue's cover image;
- Appropriate Supporting Information (Video, audio or data set [https://jp.msubmit.net/cgi-bin/main.plex?form\\_type=display\\_requirements#supp](https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_requirements#supp)).

To create your 'Response to Referees' copy all the reports, including any comments from the Reviewing Editor into a Word, or similar, file and respond to each point in colour or CAPITALS and

upload this when you submit your revision.

I look forward to receiving your revised submission.

If you have any queries please reply to this email and staff will be happy to assist.

Yours sincerely,

Ian D. Forsythe  
Deputy Editor-in-Chief  
The Journal of Physiology  
<https://jp.msubmit.net>  
<http://jp.physoc.org>  
The Physiological Society  
Hodgkin Huxley House  
30 Farringdon Lane  
London, EC1R 3AW  
UK  
<http://www.physoc.org>  
<http://journals.physoc.org>

-----  
REQUIRED ITEMS:

-The Reference List must be in Journal format [https://jp.msubmit.net/cgi-bin/main.plex?form\\_type=display\\_requirements#refs](https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_requirements#refs)

-Please upload separate high quality figure files via the submission form.

-Author profile(s) must be uploaded via the submission form. Authors should submit a short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more. A group photograph of all authors is also acceptable, providing the biography for the whole group does not exceed 150 words.

-----  
EDITOR COMMENTS

Reviewing Editor:

This manuscript has been evaluated by the Reviewer and the Reviewing Editor. Although both find the manuscript is of interest to general readers, the Reviewer has raised several concerns need to be addressed. In addition, the Reviewing Editor has the following comments.

General comments:

1. Abstract needs a major revision to cover key points (i.e., white and brown adipose tissue, thermogenesis, obesity and CVD) that are discussed in the manuscript.
2. A paragraph in the Introduction highlighting key issues to be presented in the main text is highly recommended.
3. The connection between the sections on the obesity and CVD mouse models with the key points discussed in the manuscript is not immediately clear. It is recommended to highlight the use of those models for the studies of white and brown adipose tissue dysfunction in the corresponding text.
4. Consider revising the text under "Adaptive mechanisms of sustained cold acclimatization" with focus on consequences of the aberrant adaptation to adipose dysfunction and metabolic dysregulation.
5. Given that the manuscript covers a variety of related topics, a concluding remark on the discussed issues would help the readers to better appreciate the manuscript.
6. Key message conveyed in the graphical abstract is too simplified; making it difficult to appreciate its pertinence to the key points of the manuscript.

Specific comments:

1. The last sentence in the Introduction seems to be redundant to the second sentence and is advised to revise.
2. P. 4, an introductory statement of the discussions on both obesity and CVD mouse models for the study of adipose tissue in obesity and/or CVD are recommended.
3. Advantage and limitation of the use of the mouse models for the studies on obesity and CVD should be discussed.
4. Some abbreviations are used with no proper definition (e.g. PPAR on p. 3, KO on p. 5). Please double check the text to ensure all abbreviations are properly defined.
5. Some general statements in the "Outlook" are recommended to be further elaborated with examples.

-----  
REFEREE COMMENTS

Referee #2:

This is a well-written paper on various adipose tissues, energy metabolism and cardiometabolic health.

The paper covers a considerable amount of info, but it is thorough with up-to-date discussions of research findings, and discussions on the usage of mice models to study adipose dysfunctions and cardiometabolic health.

The authors should consider revising the title to better reflect the broader content of the paper.

The very last sentence suggests research targeting endothelial cells of the vessels or the myocardium "...could contribute to the global metabolic improvement expected in therapeutic against obesity and CVD." This conclusion may be a little premature, given the considerable gap of knowledge about EAT, PAT and PVAT.

#### MINOR COMMENTS:

Abstract: Change focusses to focuses.

Page 7, last paragraph: "...lipids ender the blood stream.." Change ender to enter.

Author contributions: Unclear from this text who of the authors prepared manuscript and figures, and who commented: "The manuscript and figures were prepared by MG and HJ and KJP and AB edited and commented on text and figures." (E.g., change to "...by MG and HJ, while KJP and AB..."?)

Fig 2, legend: Should several myopathy be severe myopathy?

Fig 3, legend: Change calory to calorie.

Page 11, second para: "BAT activation reduces cholesterol levels in hypercholesterolemic patients and increases lipid turnover in obese individuals. While these human data are very much in line with studies in mice [50]...."

Please move the reference after the first sentence (or insert reference for the first sentence).

---

END OF COMMENTS

**Confidential Review**

**02-Jun-2021**

---



Point-by-point reply: JP-SR-2021-281979

Editorial comments:

The image files from the previous version are retained on the system. Please ensure you replace or remove any files that have been revised. Your revised submission should include:

- A Word file of the complete text (including figure legends any Tables);
- An Abstract Figure (with legend in the Article file)
- Each figure as a separate, high quality, file;
- A full Response to Referees;
- A copy of the manuscript with the changes highlighted.
- Author profile. A short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more.

You may also upload:

- A 'Cover Art' file for consideration as the Issue's cover image;
- Appropriate Supporting Information (Video, audio or data set [https://jp.msubmit.net/cgi-bin/main.plex?form\\_type=display\\_requirements#supp](https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_requirements#supp)).

To create your 'Response to Referees' copy all the reports, including any comments from the Reviewing Editor into a Word, or similar, file and respond to each point in colour or CAPITALS and upload this when you submit your revision.

-----  
REQUIRED ITEMS:

-The Reference List must be in Journal format [https://jp.msubmit.net/cgi-bin/main.plex?form\\_type=display\\_requirements#refs](https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_requirements#refs)

-Please upload separate high quality figure files via the submission form.

-Author profile(s) must be uploaded via the submission form. Authors should submit a short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more. A group photograph of all authors is also acceptable, providing the biography for the whole group does not exceed 150 words.



**Reviewing Editor:**

1. Abstract needs a major revision to cover key points (i.e., white and brown adipose tissue, thermogenesis, obesity and CVD) that are discussed in the manuscript.

RESPONSE: Thank you for this remark. We have revised the abstract to read: "Obesity is a medical disorder caused by multiple mechanisms of dysregulated energy balance. A major outcome of obesity is an increased risk to develop diabetic complications and cardiovascular disease. While a better understanding of the molecular mechanisms linking obesity, insulin resistance, and cardiovascular disease is needed, translational research of the human pathology is hampered by the available cell and animal model systems. Major barriers are the species differences in energy balance, adipose tissue physiology, and vascular biology, especially related to white and brown adipocytes, adipose tissue browning, and thermogenesis. This review focusses on advantages and limitations of the mouse models for the study of cardiometabolic diseases and discusses recent insight into new mechanisms linking energy metabolism and cardiometabolic health. We discuss the fundamental biology of adipocytes in white adipose tissue in obesity. On the other hand, thermogenic adipocytes found in brown adipose tissue improve metabolic health. We review the effects of white and thermogenic adipocytes on energy balance and discuss the endocrine influence of adipocytes in the control of vascular and perivascular function, inflammation, and the development of cardiovascular disease."

2. A paragraph in the Introduction highlighting key issues to be presented in the main text is highly recommended.

RESPONSE: Thank you for this remark. We have now included: "This review focusses on the biology of adipocytes, as these cells are critical pillars of a healthy metabolism. We discuss the mechanisms by which adipocyte dysfunction in obesity contributes to the development of cardiovascular disease in humans, and how these processes can be studied in the mouse as the most important model organism. Adipocytes are found throughout the body, displaying a broad range of phenotypes depending on developmental origin, functional plasticity, and environmental conditions. We review the biology of classical white as well as of thermogenic adipocytes, also considering the highly diverse nature of perivascular adipose tissue (PVAT)."

3. The connection between the sections on the obesity and CVD mouse models with the key points discussed in the manuscript is not immediately clear. It is recommended to highlight the use of those models for the studies of white and brown adipose tissue dysfunction in the corresponding text.

RESPONSE: Thank you for this remark. It was stated that for studying the connection between adipocyte function, obesity, and CVD research relies on using mouse models, which is elaborated on in this paragraph. We have combined the two mouse model paragraphs and made the relevance of these considerations clearer at the beginning: "While the association of adipocyte function, obesity, and CVD in humans is evident, it is important to realize that using the mouse as a model organism has limitations. In most cases, genetic and/or dietary interventions are required to induce obesity or CVD. Most obesity models do not develop CVD, and vice versa."

4. Consider revising the text under "Adaptive mechanisms of sustained cold acclimatization" with focus on consequences of the aberrant adaptation to adipose dysfunction and metabolic dysregulation.

RESPONSE: We have revised the paragraph to contain the consequences of aberrant adaptation: "In the absence of Nfe2l1, brown and beige adipocytes progressively lose their thermogenic capacity, as cellular stress originating but not limited to ER drives adipocyte dysfunction. This leads to whitening of BAT and diminished adipose tissue browning with marked inflammation of the fat pads [79]. This does not necessarily lead to a reduction in energy expenditure, rather the organism adapts to the absence of NST. While HFD-induced weight gain is similar, mice deficient in adipocyte Nfe2l1 are more glucose intolerant and insulin resistant. How Nfe2l1 impacts on CVD is an active area of investigation."

5. Given that the manuscript covers a variety of related topics, a concluding remark on the discussed issues would help the readers to better appreciate the manuscript.

RESPONSE: We have now added a subheading "7. Concluding remarks" at the end of the manuscript.

6. Key message conveyed in the graphical abstract is too simplified; making it difficult to appreciate its pertinence to the key points of the manuscript.

RESPONSE: We have revised the graphical abstract.

7. The last sentence in the Introduction seems to be redundant to the second sentence and is advised to revise.

RESPONSE: Amended to "Thus, the increasing prevalence of obesity, particularly at younger ages, is prolonging the lifetime exposure to insulin resistance, T2D, and associated cardiovascular complications."

8. P. 4, an introductory statement of the discussions on both obesity and CVD mouse models for the study of adipose tissue in obesity and/or CVD are recommended.

RESPONSE: Pursuant to reviewing editor point #3 we have added the statement: "While the association of adipocyte function, obesity, and CVD in humans is evident, it is important to realize that using the mouse as a model organism has limitations. In most cases, genetic and/or dietary interventions are required to induce obesity or CVD. Most obesity models do not develop CVD, and vice versa."

9. Advantage and limitation of the use of the mouse models for the studies on obesity and CVD should be discussed.

RESPONSE: Thanks for pointing this out. This is included in the paragraph "Mouse models for studying adipocyte function in obesity and CVD"

10. Some abbreviations are used with no proper definition (e.g. PPAR on p. 3, KO on p. 5). Please double check the text to ensure all abbreviations are properly defined.

RESPONSE: We apologize for these inaccuracies. We have thoroughly reviewed and revised the abbreviations.

11. Some general statements in the "Outlook" are recommended to be further elaborated with examples.

RESPONSE: We have markedly revised the outlook to include this notion.

**Referee #2:**

This is a well-written paper on various adipose tissues, energy metabolism and cardiometabolic health. The paper covers a considerable amount of info, but it is thorough with up-to-date discussions of research findings, and discussions on the usage of mice models to study adipose dysfunctions and cardiometabolic health.

1. The authors should consider revising the title to better reflect the broader content of the paper.

**RESPONSE:** We have revised the title to "Adipocyte function and the development of cardiometabolic disease".

2. The very last sentence suggests research targeting endothelial cells of the vessels or the myocardium "...could contribute to the global metabolic improvement expected in therapeutic against obesity and CVD." This conclusion may be a little premature, given the considerable gap of knowledge about EAT, PAT and PVAT.

**RESPONSE:** We have markedly revised the outlook to include this notion.

3. Abstract: Change focusses to focuses.

**RESPONSE:** The reviewer might have overlooked that we are using the verb and not the noun.

4. Page 7, last paragraph: "...lipids enter the blood stream.." Change enter to enter.

**RESPONSE:** Thank you for spotting this typo.

5. Author contributions: Unclear from this text who of the authors prepared manuscript and figures, and who commented: "The manuscript and figures were prepared by MG and HJ and KJP and AB edited and commented on text and figures." (E.g., change to "...by MG and HJ, while KJP and AB..."?)

**RESPONSE:** We have clarified the statement.

6. Fig 2, legend: Should several myopathy be severe myopathy?

**RESPONSE:** Thank you for spotting this typo.

7. Fig 3, legend: Change calory to calorie.

**RESPONSE:** Thank you for spotting this typo.

8. Page 11, second para: "BAT activation reduces cholesterol levels in hypercholesterolemic patients and increases lipid turnover in obese individuals. While these human data are very much in line with studies in mice [50]...". Please move the reference after the first sentence (or insert reference for the first sentence).

**RESPONSE:** Thank you for pointing out this mix-up. We have revised the sentence and moved the reference up to read: "In humans, BAT activity is linked to lower BMI and improved insulin sensitivity [50]. While these obesity data are in line with studies in mice, the outcomes of cold exposure on CVD are complicated by the mouse models used."

Dear Dr Bartelt,

Re: JP-SR-2021-281979R1 "Adipocyte function and the development of cardiometabolic disease" by Maude Giroud, Henrika Jodeleit, Kacey June Prentice, and Alexander Bartelt

Thank you for submitting your invited Symposium Review to The Journal of Physiology. It has been assessed by a Reviewing Editor and by 1 expert referee and I am pleased to tell you that it is considered to be acceptable for publication following satisfactory revision.

Please advise your co-authors of this decision as soon as possible.

The reports are copied at the end of this email. Please address all of the points and incorporate all requested revisions, or explain in your Response to Referees why a change has not been made.

**NEW POLICY:** In order to improve the transparency of its peer review process The Journal of Physiology publishes online as supporting information the peer review history of all articles accepted for publication. Readers will have access to decision letters, including all Editors' comments and referee reports, for each version of the manuscript and any author responses to peer review comments. Referees can decide whether or not they wish to be named on the peer review history document.

I hope you will find the comments helpful and have no difficulty in revising your manuscript within 4 weeks.

Your revised manuscript should be submitted online using the links in Author Tasks Link Not Available. This link is to the Corresponding Author's own account, if this will cause any problems when submitting the revised version please contact us.

The image files from the previous version are retained on the system. Please ensure you replace or remove any files that have been revised. Your revised submission should include:

- A Word file of the complete text (including figure legends any Tables);
- An Abstract Figure (with legend in the Article file)
- Each figure as a separate, high quality, file;
- A full Response to Referees;
- A copy of the manuscript with the changes highlighted.
- Author profile. A short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more.

You may also upload:

- A 'Cover Art' file for consideration as the Issue's cover image;
- Appropriate Supporting Information (Video, audio or data set [https://jp.msubmit.net/cgi-bin/main.plex?form\\_type=display\\_requirements#supp](https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_requirements#supp)).

To create your 'Response to Referees' copy all the reports, including any comments from the Reviewing Editor into a Word, or similar, file and respond to each point in colour or CAPITALS and

upload this when you submit your revision.

I look forward to receiving your revised submission.

If you have any queries please reply to this email and staff will be happy to assist.

Yours sincerely,

Ian D. Forsythe  
Deputy Editor-in-Chief  
The Journal of Physiology  
<https://jp.msubmit.net>  
<http://jp.physoc.org>  
The Physiological Society  
Hodgkin Huxley House  
30 Farringdon Lane  
London, EC1R 3AW  
UK  
<http://www.physoc.org>  
<http://journals.physoc.org>

-----  
EDITOR COMMENTS

Reviewing Editor:

Both the Reviewing Editor and the Reviewer are satisfactory with the responses by the authors. Quality of the revised manuscript is much improved.

Senior Editor:

Congratulations on a thorough revision. The figures are excellent and the text very readable. I have one important request to improve the appeal to a wide readership - namely to re-write your abstract to contain more factual information. Please avoid phrases like " We review the effects of white and thermogenic adipocytes on..." and instead state a summary of your findings. Then finish with a clear concluding sentence. I look forward to reading your final minor revision.

-----  
REFEREE COMMENTS

Referee #2:

Thank you for the responses to the review.

Ref previous minor comment #3 (focusses vs. focuses): No, I didn't mistake the word for a noun instead of a verb. The unusual/rare original spelling is maybe allowed in British English, but thanks anyway for changing it.

---

END OF COMMENTS

**1st Confidential Review**

**11-Aug-2021**

---



Institut für Prophylaxe und Epidemiologie der Kreislaufkrankheiten  
Max-Lebsche-Platz 30, 81377 München

Journal of Physiology  
Editorial Office

**Leitung / Direktor**  
Univ.-Prof. Dr. med. Christian Weber

**Ihr Ansprechpartner**  
Univ.-Prof. Dr. Alexander Bartelt  
Professor of Cardiovascular Metabolism  
Tel. +49 89 4400 43905  
Fax +49 89 4400 54298  
Cell +49 160 954 11769  
alexander.bartelt@med.uni-muenchen.de  
www.kreislaufinstitut.de

**RE: Revised version JP-SR-2020-280914 Symposium Review Commissioned  
Manuscript for The Journal of Physiology - Invited review "Adipose tissue browning  
and cardiometabolic health"**

Dear editors

please find enclosed our revised version of the review on obesity, cardiovascular disease, and  
adipose tissue physiology. We are deeply grateful for this opportunity.

We have responded to the requests by the senior editor:

*Congratulations on a thorough revision. The figures are excellent and the text very readable. I  
have one important request to improve the appeal to a wide readership - namely to re-write your  
abstract to contain more factual information. Please avoid phrases like " We review the effects  
of white and thermogenic adipocytes on..." and instead state a summary of your findings. Then  
finish with a clear concluding sentence. I look forward to reading your final minor revision.*

**RESPONSE: We have revised the abstract according to the requests and suggestions by the  
senior editor.**

Please contact me with any questions you may have.

Yours sincerely



Univ.-Prof. Dr. Alexander Bartelt  
Professor of Cardiovascular Metabolism  
Principal Investigator Helmholtz Diabetes Center  
ERC & DZHK Researcher

**Datum**

25.08.2021

**Ihr Zeichen**

xxxx

**Unser Zeichen**

xxxx

**Vorstand**

Ärztlicher Direktor:  
Prof. Dr. Markus M. Lerch  
(Vorsitz)

Kaufmännischer Direktor:  
Markus Zendler

Pflegedirektor (komm.):  
Alfred Holderied

Vertreter der Medizinischen Fakultät:  
Prof. Dr. med. dent. Reinhard Hickel  
(Dekan)

Institutionskennzeichen:  
260 914 050

Umsatzsteuer-ID:  
DE813536017

Das Klinikum der Universität  
München ist eine Anstalt des  
Öffentlichen Rechts



Dear Professor Bartelt,

Re: JP-SR-2021-281979R2 "Adipocyte function and the development of cardiometabolic disease" by Maude Giroud  
Henrika Jodeleit  
Kacey June Prentice  
Alexander Bartelt

I am pleased to tell you that your Symposium Review article has been accepted for publication in The Journal of Physiology, subject to any modifications to the text that may be required by the Journal Office to conform to House rules.

\*\*\*IMPORTANT\*\*\*

We seem to be missing a figure legend to accompany your abstract figure. Our typesetters will require this. Please can you send a Word file of the abstract figure legend to us as soon as possible to: [jp@physoc.org](mailto:jp@physoc.org)  
Thank you.

**NEW POLICY:** In order to improve the transparency of its peer review process The Journal of Physiology publishes online as supporting information the peer review history of all articles accepted for publication. Readers will have access to decision letters, including all Editors' comments and referee reports, for each version of the manuscript and any author responses to peer review comments. Referees can decide whether or not they wish to be named on the peer review history document.

The last Word version of the paper submitted will be used by the Production Editors to prepare your proof. When this is ready you will receive an email containing a link to Wiley's Online Proofing System. The proof should be checked and corrected as quickly as possible.

All queries at proof stage should be sent to [tjp@wiley.com](mailto:tjp@wiley.com)

The accepted version of the manuscript is the version that will be published online until the copy edited and typeset version is available. Authors should note that it is too late at this point to offer corrections prior to proofing. Major corrections at proof stage, such as changes to figures, will be referred to the Reviewing Editor for approval before they can be incorporated. Only minor changes, such as to style and consistency, should be made a proof stage. Changes that need to be made after proof stage will usually require a formal correction notice.

Are you on Twitter? Once your paper is online, why not share your achievement with your followers. Please tag The Journal (@jphysiol) in any tweets and we will share your accepted paper with our 22,000+ followers!

Yours sincerely,

Ian D. Forsythe  
Deputy Editor-in-Chief  
The Journal of Physiology  
<https://jp.msubmit.net>

<http://jp.physoc.org>  
The Physiological Society  
Hodgkin Huxley House  
30 Farringdon Lane  
London, EC1R 3AW  
UK  
<http://www.physoc.org>  
<http://journals.physoc.org>

-----  
Comments:

Senior Editor:

Many thanks for that final point - I look forward to reading your article in press.

Please provide an abstract figure legend, as mentioned above.

-----  
**\* IMPORTANT NOTICE ABOUT OPEN ACCESS \***

Information about Open Access policies can be found here  
<https://physoc.onlinelibrary.wiley.com/hub/access-policies>

To assist authors whose funding agencies mandate public access to published research findings sooner than 12 months after publication The Journal of Physiology allows authors to pay an open access (OA) fee to have their papers made freely available immediately on publication.

You will receive an email from Wiley with details on how to register or log-in to Wiley Authors Services where you will be able to place an OnlineOpen order.

You can check if your funder or institution has a Wiley Open Access Account here  
<https://authorservices.wiley.com/author-resources/Journal-Authors/licensing-and-open-access/open-access/author-compliance-tool.html>

Your article will be made Open Access upon publication, or as soon as payment is received.

If you wish to put your paper on an OA website such as PMC or UKPMC or your institutional repository within 12 months of publication you must pay the open access fee, which covers the cost of publication.

OnlineOpen articles are deposited in PubMed Central (PMC) and PMC mirror sites. Authors of OnlineOpen articles are permitted to post the final, published PDF of their article on a website, institutional repository, or other free public server, immediately on publication.

Note to NIH-funded authors: The Journal of Physiology is published on PMC 12 months after publication, NIH-funded authors DO NOT NEED to pay to publish and DO NOT NEED to post their accepted papers on PMC.

