

Reviewer 3

Comments:

This short communication looks mainly like a kind of review, with a focus primarily on the examination of (immediate) neurophysiological responses to the built environment (Introduction 1st paragraph, line 6). This is despite the author's claim to have a main thrust intended to be directed towards studying *chronic* exposure to stress-inducing architectural forms (Abstract line 13).

This raises two main questions:

(I) Originality in the submitted manuscript is sought mainly in the author's claim to study 'the impact of long-term or chronic exposure to stress-inducing architectural features on human health... yet to (be) examine(d)' (Abstract). The part of the manuscript addressing what should be the principal part of the work is however a relatively superficial account on pages 6 and 7. I cannot find any account of for instance empirical results of the author's about the specific topic of chronic exposure and its effects. Instead, the author gives again a review; at best making some "suggestions" (last paragraph of section 3).

That long-term exposure to stress can lead to chronic effects will be no surprise to any reader and is readily mentioned in the literature on stress, e.g: Pretty J, Peacock J, Sellens M, Griffin M. 2005, The mental and physical health outcomes of green exercise, *International Journal of Environmental Health Research* **15**, 319–37. [PubMed: 16416750].

One key Allostasis paper early on by McEwen 1998 describes *Stress research* as: "understanding of psychological, physiological and behavioural mechanisms leading from stress exposure to stress response and the development of stress-related health problems".

McEwen BS: Stress, Adaptation, and Disease: Allostasis and Allostatic Load. *Ann N Y Acad Sci* 1998, 840(1):33-44.

Guidi *et al.* 2021 [28] has recently given a systematic review of Allostatic Load and Its Impact on Health, where Allostatic Load is explicitly 'the cumulative burden of chronic stress and life events'.

I look forward to a manuscript from the author where perhaps the Introduction could be formed starting with section 3 of the present manuscript, but then containing the results of original investigations of chronic stress.

(II) We are promised (middle of Abstract) "a conceptual framework for understanding the relationship between chronic exposure to stress-inducing architectural forms and chronic inflammation". The author appears, in making his review (sections 1 & 2) of neurophysiological responses to the built environment, to present a rather restricted version of the promised "conceptual framework" with a particular bias towards "Stress responses ... empirically measured" (Section 1, 2nd paragraph) and explained (section 2, figure 2 using clinical biomarkers).

But, if I understand correctly, stress response is not merely registered with clinical biomarkers. Indeed, stress responses can be both *affective*, *behavioural* or biological. [Cohen S, Kessler RC, Gordon LU: Strategies for measuring stress in studies of psychiatric and physical disorders. In: Measuring stress: a guide for health and social scientists. edn. Oxford; New York, N.Y: Oxford University Press; 1995: 3-26].

Some researchers may consider affective and behavioural responses to be "less objective" and "more difficult to measure" than biomarkers. On the other hand, arguably, a person's stress experience will be dominated by these affective and behavioural effects, rather than changes in their biomarkers. There is, however, a

substantial body of research employing the psychometric measurement theory of Rasch which can provide objective measures of affective and behavioural constructs: both of the level of stress presented by a stressor (e.g. an architectural feature) and the sensitivity of a person to become stressed. These stressor and person-related attributes should be able to be modelled separately in terms of explanatory variables, such as in construct specification equations.

An example of recent stress research employing Rasch measurement theory is the work of Hadžibajramović E, Ahlborg G, Håkansson C, Lundgren-Nilsson Å, Grimby-Ekman A: Affective stress responses during leisure time: Validity evaluation of a modified version of the Stress-Energy Questionnaire. Scand J Public Health 2015, doi: 1403494815601552, first published on Sept. 21, 2015.

The author therefore needs to complement the "biomarker" focus in his conceptual framework with accounts covering affective and behavioural responses to stress with modern measurement theory.

Overall, to make the manuscript acceptable, I need to see convincing responses to these two main questions (I) and (II)

Response:

Dear Reviewer,

Thank you for your thoughtful review of this manuscript. The current version of the document has been substantially revised and improved as a result of your insightful comments and valuable feedback.

The paper has been restructured and an in depth analysis of the methods used to measure allostatic load has been conducted and incorporated into the revised article. These revisions provide the reader with practical insight into how to measure the proposed relationship between stress-inducing architectural forms and allostatic load. A particularly interesting point that emerged from this revision process was that the neuroarchitectural studies that measure stress responses to architectural forms used markedly different biomarkers to those that measure allostatic load. Consequently, the revised manuscript advises that, given the different measurement techniques, while the research on stress-inducing architectural forms may be capturing allostatic activity, the methods used are not appropriate for measuring the long-term impacts of these architectural forms on allostatic load. Therefore, the paper now concludes that further research is needed to determine whether these stress responses are leading to allostatic overload, using the methods highlighted in the revised manuscript.

While the paper does not incorporate original data from empirical research, the insights provided by the interdisciplinary review are - it is hoped - sufficiently novel and capable of informing future research in an emerging field. It is hoped that the revisions now provide a more robust conceptual framework for understanding the connection between stress-inducing architectural features and allostatic load, highlight certain issues with assuming a connection between stress-inducing architectural features and allostatic load given the differing approaches to measurement, and provides insight into how a future longitudinal public health study into the relationship between architecture and allostatic load could be conducted.

Thank you once again for your comments, the manuscript has substantially benefited from your considered insights. Please note that I have carefully considered each of your comments and have attempted to address them all. A more detailed point-by-point response is attached below.

Kind regards.

Matrix:

Reviewer Comment	Author Response
This short communication looks mainly like a kind of review, with a focus primarily on the examination of (immediate) neurophysiological responses to the built environment (Introduction 1st paragraph, line 6). This is despite the author's claim to have a main thrust intended to be directed towards studying <i>chronic</i> exposure to stress-inducing architectural forms (Abstract line 13).	In response, I have incorporated the suggestion and expanded the original article. While the paper does review literature from multiple disciplines, it does so to present a novel argument that opens up scope for future research. Rather than being solely a review, this paper now suggests that there is a gap in the literature (i.e., that while a connection between architectural form and acute stress responses has been made, the clinical biomarkers used to measure stress in neuroarchitectural studies differ substantially from those used to measure allostatic load, therefore the effects of architectural form on allostatic load have not been studied in their own right). As such, I believe the paper goes beyond a review and does provide novel insight into an emerging issue. The paper presents new and original material on the potential impact of architectural form on allostatic load, which has thus far been unexplored. This, I believe, is a novel and significant development for the field of neuroarchitecture.
Originality in the submitted manuscript is sought mainly in the author's claim to study 'the impact of long-term or chronic exposure to stress-inducing architectural features on human health... yet to (be) examine(d)' (Abstract). The part of the manuscript addressing what should be the principal part of the work is however a relatively superficial account on pages 6 and 7. I cannot find any account of for instance empirical results of the author's about the specific topic of chronic exposure and its effects. Instead, the author gives again a review; at best making some "suggestions" (last paragraph of section 3).	This point is well taken. In response, I have incorporated the suggestion and restructured the original article. The new article highlights the observation that while the observed stress responses to particular architectural forms may indicate allostatic activity, the clinical biomarkers used to measure stress in neuroarchitectural studies differ substantially from those used to measure allostatic load. Therefore, the paper now concludes that further research is needed to determine whether these stress responses are leading to allostatic overload. Moreover, the paper goes on to review the experimental design of allostatic overload research to reveal two primary methods used to measure allostatic overload: biomarkers and clinimetrics. Additionally, I have made suggestions as to how these methods may be applied to future research examining the impact of architectural form on allostatic overload.

That long-term exposure to stress can lead to chronic effects will be no surprise to any reader and is readily mentioned in the literature on stress, e.g: Pretty J, Peacock J, Sellens M, Griffin M. 2005, The mental and physical health outcomes of green exercise, <i>International Journal of Environmental Health Research</i> 15, 319–37. [PubMed: 16416750]. One key Allostasis paper early on by McEwen 1998 describes <i>Stress research</i> as: "understanding of psychological, physiological and behavioural mechanisms leading from stress exposure to stress response and the development of stress-related health problems". McEwen BS: Stress, Adaptation, and Disease: Allostasis and Allostatic Load. <i>Ann N Y Acad Sci</i> 1998, 840(1):33–44. Guidi <i>et al.</i> 2021 [28] has recently given a systematic review of Allostatic Load and Its Impact on Health, where Allostatic Load is explicitly 'the cumulative burden of chronic stress and life events'.	As mentioned above, this is well taken and investigating this assumption that stress can lead to chronic effects has led to an interesting insight which is now incorporated into the revised manuscript From this additional research, I observed that although the connection between architectural form and stress, and stress and allostatic overload may appear obvious, this paper now highlights a gap in this logic. Namely, the revised article highlights the observation that while the observed stress responses to particular architectural forms may indicate allostatic activity, the clinical biomarkers used to measure stress in neuroarchitectural studies differ substantially from those used to measure allostatic load. Consequently, the revised manuscript advises that, given the different measurement techniques, the research on stress-inducing architectural forms may not be capturing the long-term impacts of these architectural forms on allostatic load. Therefore, the paper now concludes that further research is needed to determine whether these stress responses are leading to allostatic overload.
I look forward to a manuscript from the author where perhaps the Introduction could be formed starting with section 3 of the present manuscript, but then containing the results of original investigations of chronic stress.	I have since rewritten the manuscript to start with section 3 and then continue to outline possible experimental methodologies and future research techniques which I hope to employ in the future.
We are promised (middle of Abstract) "a conceptual framework for understanding the relationship between chronic exposure to stress-inducing architectural forms and chronic inflammation". The author appears, in making his review (sections 1 & 2) of neurophysiological responses to the built environment, to present a rather restricted version of the promised "conceptual framework" with a particular bias towards "Stress responses ... empirically measured" (Section 1, 2nd paragraph) and explained (section 2 , figure 2 using clinical biomarkers. But, if I understand correctly, stress response is not merely registered with clinical biomarkers. Indeed, stress responses can be both <i>affective, behavioural</i> or biological. [Cohen S, Kessler RC, Gordon LU: Strategies for measuring stress in studies of psychiatric and physical disorders. In: Measuring	This is an interesting point. I have aimed to address this by incorporating the concept of clinimetrics. Here clinimetrics is a known methodology for evaluating allostatic load that complements biomarkers to provide a more comprehensive analysis of stress. I have specifically incorporated research from Cohen et al., 2013, 2014 as well as other authors who illustrate the significance of affective and behavioural responses on allostatic load (See page 10).

stress: a guide for health and social scientists. edn. Oxford; New York, N.Y: Oxford University Press; 1995: 3-26].

Some researchers may consider affective and behavioural responses to be "less objective" and "more difficult to measure" than biomarkers. On the other hand, arguably, a person's stress experience will be dominated by these affective and behavioural effects, rather than changes in their biomarkers. There is, however, a substantial body of research employing the psychometric measurement theory of Rasch which can provide objective measures of affective and behavioural constructs: both of the level of stress presented by a stressor (e.g. an architectural feature) and the sensitivity of a person to become stressed. These stressor and person-related attributes should be able to be modelled separately in terms of explanatory variables, such as in construct specification equations.

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