

Responses to reviewers

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Article title: Does pupillometry provide a valid measure of spatial attentional bias (pseudoneglect)?

Authors: Nicola E Burns and Robert D McIntosh

Journal title: PCI-RR

Comments from the Reviewers:

Reviewer 1:

Burns and McIntosh describe their attempt to replicate our paper from 2022 in Cortex (Strauch, Romein, Naber, Van der Stigchel & Ten Brink), where we introduced the, what the authors call, split-field pupillometry task (which is a great name!), and where we showed that the pupil responds stronger to the brightness on the left than to the brightness on the right, indicating pseudoneglect. Burns and McIntosh, however, find rightward not leftward biases in pupil light responses. As they tracked the right eye, whereas we tracked the left eye in our Experiment 1, this suggests that effects of our original Experiment 1 are likely confounded by the differences in illumination to the eyes rather than attention. The authors went further by reanalyzing our old data, reproducing the overall leftward bias we observed using the average of both eyes in Experiment 2, which suggest that both attention and a physiological explanation contributed to the effects reported. As the left eye here showed a substantial leftward bias in Exp 2 whilst the right didn't (resulting in overall leftward bias), this shows an important issue in the split-field pupillometry task: the average of both eyes has to be taken to investigate pseudoneglect. The authors clearly applied rigor in their replication attempt and we think that this manuscript will be helpful in developing the earlier proposed method further. Yet, we have a couple of points that will align the original and the now preregistered replication attempt more closely and will be necessary to allow for a closer replication than the original data reported here.

1. As an exploratory analysis (we would leave this to the authors), we would be curious whether sensitivity is different if a longer interval is used instead of the constriction amplitude alone. In our second paper (with patients; Ten Brink et al., 2023) we found better sensitivity when considering more data points.

As suggested, we checked whether sensitivity would be different if a longer interval was used (using the averaging method described in Ten Brink et al. 2023) instead of the constriction amplitude alone. However, the averaging method was considerably less sensitive than focusing on the maximum constriction amplitude. In addition, the maximum constriction amplitude after stimulus onset corresponds better to the pupillary light reflex (i.e., initial transient response to illumination), which is where we are placing the theoretical emphasis in this experiment. It is possible that average pupil size over the response period could be explored at Stage 2, but we have not registered this plan in the Stage 1 RR.

2. About the inclusion of a vertical condition in our paper, it is stated that "Strauch and colleagues had used this as a 'control condition' in their second experiment, perhaps on the assumption that there would be no bias for the vertical dimension." However, we were aware that (very strong) effects were to be expected (described as pupil anisotropies). We

did not focus on these, as the vertical condition was merely added as a sanity check, to confirm the absence of a correlation with the left-right greyscales bias. This was, unfortunately, not clearly communicated in our paper so we understand the interpretation of the authors. That being said, we did not assume an attentional bias towards the upper field. Attention might contribute here, but anisotropies in receptors or visual areas in the brain should not be overlooked here as potential contributors. For instance, the SC is topographically organized in a way that might contribute to such anisotropies (Wang & Munoz, 2018, PNAS; reviewed in Strauch, Wang, Einhäuser, Van der Stigchel & Naber, 2022, TINS on page 643).

Thank you very much for clarifying this. We have modified our manuscript on p4 and p8 to make it more clear what factors might potentially account for the upward pupillary constriction bias.

3. Related to this, for H3, it would be interesting (and extending the experiment beyond a replication) to add a rotated version of the greyscales task that allows to assess attentional up/downward biases. These could then be correlated with the up/down differences in pupil constriction. Whilst this doesn't imply that all anisotropies in the light response are due to attention, any covariation with the greyscales task could establish such attentional differences for the upper/lower fields (even though, as the authors correctly state, the eyes are not vertically centered).

Thank you for pointing this out. The inclusion of vertical pupillometry was intended specifically to clarify whether the observed vertical pupillary constriction bias persists when participants' eyes are centred vertically with respect to the screen, and we now make this more evident with some added text on p8. However, even if it does persist, we think that it will remain equivocal whether it is attributable to attentional or neurophysiological factors. This is due to inherent differences in the extent of the upper and lower visual fields, and possibly differential cortical and subcortical representations, as mentioned in the reviewer's point (2), and as we now note on p4. Similar ambiguities would apply to the interpretation of a vertical greyscales task. On balance, we prefer not to administer the vertical greyscales task, as this could give the false impression that we are measuring attention in the vertical dimension, which we are not confident that this task would unambiguously do.

4. The distance from eye position to monitor is different in the currently described study (79cm) from ours (67.5cm). This is important as pseudoneglect is described to diminish or even flip from left to right with more leftward biases reported closer by (e.g., Heber, Siebertz, Wolter, Kühlen, & Fimm, 2010, Brain and Cognition). An adjustment to the same distance seems therefore sensible. Similarly, the monitor should be of a similar size as the original monitor to control for possible effects induced by the stimuli covering larger/smaller parts of the visual field. Reduced leftward biases at further distances could otherwise be an indication that the split-field pupillometry task captures pseudoneglect. As suggested, we have adjusted the monitor's position to a more similar distance within peripersonal space as in the original paper. However, we are using a slightly closer distance (600 mm) to match the original setup's visual angle. See subsequent detail changes on p11.

5. It should be discussed whether the tower mount tracker results in restricted view to the periphery and additional reflections relative to the table-mounted tracker we used in both Cortex papers.

For this RR, we are using a desktop mount arrangement, as in Strauch et al. (2022).

6. The authors state the number of trials that must be absolved per stimulus. We assume that these will be presented in random order across conditions, as in our original paper. This should be described.

Thank you for bringing this to our attention. We have now described this on p13.

7. It should be described whether age-restrictions are taken as an inclusion criterion. Preferably, the sample should be roughly age-matched as in the original study of Strauch et al. (2022). In the study of Ten Brink et al. (2023) the healthy control group was (partially) of older age than the group in the study of Strauch et al. (2022), and in Ten Brink et al., (2023), we found increasingly less leftward and more rightward pupillometric pseudoneglect estimates (albeit not significant) – in line with the literature on age-effects seen on others measures of pseudoneglect.

To maintain comparability with the sample used in the original research, we will restrict our age range to 18 – 50. This is now stated on p10.

8. If the hypothesis on at least partial anisocoria is correct (looking at the reanalysis of our data and the data put forward for the right eye here, we would not be surprised), this necessitates caution when interpreting the effect sizes in two of our papers. Besides the Strauch et al. (2022) paper, where effect sizes might be overestimated, this would also imply that the effect size for the dissociation between patients with neglect and controls in Ten Brink et al. (2023, Cortex) would be underestimated. The latter as we here tracked the left eye for patients (with assumed rightward attentional bias) and the average of both eyes for controls. In our opinion, a short discussion hereof might also benefit those intending to use the method to assess neglect in clinical populations.

This is interesting; however, it is more suitable for discussion in the Stage 2 RR. Consequently, we will defer this discussion until that stage of the process.

9. Additionally, Teuni ten Brink, the last author on the Strauch et al. (2022) paper wrote to us to suggest that we should include a Porta test of eye dominance as an additional demographic variable of potential exploratory interest. We have now included this test, as specified on p11 and p12.

Reviewer 2

Summary

In this Registered Report, the authors focus on the recent findings by Strauch et al. (2022) that pupillary responses seem to be an index of leftward biases in visuospatial attention (pseudoneglect). They thoroughly explored the original data and conducted a preliminary replication, which did not replicate and in fact found a rightward bias. Based on this they suggested that the findings originally reported by Strauch et al. may be an artefact of the fact that they primarily reported data collected from the left eye whereas the current authors collected data primarily from the right. They suggest that ipsilateral contraction anosocoria based on heminasal retinal responsivity to light may explain the disparate

pattern of results, yet cannot fully rule out whether there is still an influence of covert attentional bias. As such, the study proposed in this registered report will explore both of these possibilities.

Review

The proposed study is exceptionally well thought out. The introduction provides a clear overview of the phenomena. They carefully considered the original data from Strauch et al., exploring which pupil size measure should be used, and accounted for chance variation in pupil constriction over the course of a full trial. After reporting the contradictory results of their replication study, they subsequently re-ran the analysis for Strauch et al.'s data by separating out the two eyes in the experiments where both were collected. In doing so they highlighted somewhat conflicting findings, and I would like to commend the authors for such a thorough revisitation of the original data.

The hypotheses, and planned analyses, were also well considered. I thought their proposed method of scoring the pupillometry data to be clever. If they simply measured pupil constriction of the left eye versus right eye, they would not be able to get to the heart of the matter – that is, whether (and to what extent) ipsilateral constriction anosocoria may account for the previous patterns of results.

The stimuli, procedure, and planned sample size are all justified and reasonable, and I would not suggest any changes. Overall this stage 1 manuscript has a logical theoretical basis, sufficient methodological detail, a sound analysis pipeline, and consideration of what a mixed pattern of results may look like.

I have only two minor comments for the authors to address:

1. In section 2.5, the authors note that the plan of analysis for the pupillary pseudoneglect hypothesis will involve calculating pupil change in the bright right vs. bright left conditions. However I could not find mention of whether this was overall pupil change across both eyes, or whether this would be calculated and examined separately for the left and right eyes (or, even less unlikely, only examined for one eye). I suspect the first option is the case but clarity on this would be appreciated.

Thank you for pointing this out. The analysis will encompass overall pupil change across both eyes. This additional detail can be found on [p14](#).

2. On page 16 the authors note the possibility that apparent pseudoneglect may not correlate with greyscales, and if this is the case it could weaken the validity of the pupillometry task as a measure of spatial attention. While I don't necessarily disagree, what of the various findings that different measures of pseudoneglect often don't correlate with each other? Attention biases may have a few different underlying mechanisms/routes (e.g., see Learmonth et al., 2015) and even if they do have a shared commonality this can be difficult to observe for a number of reasons (Chen et al., 2019). I would like to see some consideration of these matters in their report.

Thank you for highlighting this point, a short consideration of which has been added on [p16](#). We may elaborate on this general issue in the Stage 2 report, if it seems relevant to the interpretation of results.