

## Responses to Reviews

We thank the reviewers for their comments on the manuscript.

### Reviewer #1

1. **... The authors were correct to express those doubts in their manuscript; but unfortunately, because the evidence for the effect in schizophrenia is questionable, it also undermines the relevance of their own research.**

We are sympathetic to the reviewer's perspective—however, we believe that the study does make a legitimate contribution to knowledge and is worth reporting. Here, we elaborate on this rationale.

First, we emphasise that our evaluation of the literature on orientation-dependent surround suppression in schizophrenia should not be taken as evidence against the existence of the effect. Rather, we believe that, for the reasons we outline in the manuscript, the nature of the effect in schizophrenia is currently unclear. We hope that publication of this manuscript will motivate further study in this area to address the identified concerns (which are not, to our knowledge, coherently articulated elsewhere).

Second, we do not believe that the value of the study is contingent on knowledge of the expression of orientation-dependent contextual modulation in schizophrenia. The relationship between perception and schizotypy is a standalone area of research, and the publication of studies reporting the lack of such associations is an important antidote to biases and unnecessary duplication in the area.

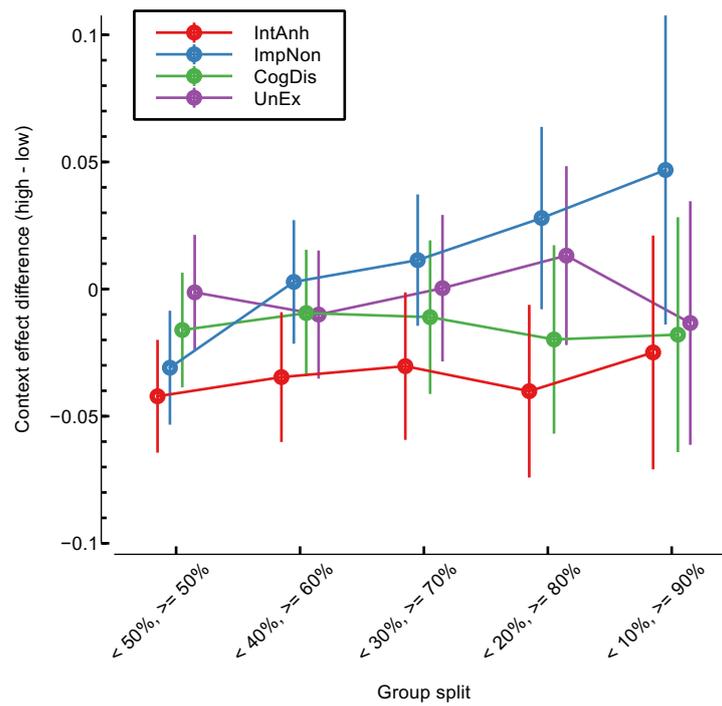
Third, we also believe that the study has value as a comprehensive quantification of a basic visual phenomenon (orientation-dependent surround suppression). The comparatively large sample size will permit future basic and applied vision studies exploring this effect to be informed by the precise estimates reported here.

2. **Because the authors speculated that there would be a significant negative correlation between an individual's score on a psychometric measure of schizotypy and his/her ability to detect the target during the visual contextual modulation task paradigm they adapted from of Serrano-Pedraza et al. (2014), they also introduced some extra experimental conditions; those conditions differed only slightly from the original ones because of a small manipulation, engineered to affect temporal processing and aimed to abolish the expected relationship between the ability to detect the target and the degree of schizotypy. Since the relationship in question could never be established in the first place, the results yielded by those extra two conditions are unfortunately totally irrelevant.**

We acknowledge that the 'leading surround' level of the temporal relationship factor is indeed uninformative given the lack of support for the fundamental prediction. We report the results in the text for completeness, referring the reader to Supplementary Material for the figures to avoid clutter.

3. **The relationship between orientation-dependent contextual modulation of visual contrast detection and its potential relationship with psychometrically defined schizotypy might of course have been obscured as the authors pointed out because "the sample contained insufficient participants with extreme scores." A quick assessment that might verify whether this concern is justified or not, can be obtained by repeating the analysis including only the 1/3 of individuals with the highest schizotypy scores and the 1/3 with the lowest scores. Based upon visual inspections of the graphs in figure 4, it seems however very unlikely that the outcome of this extra analysis would tip the balance even slightly in favor of a different outcome.**

Our concern here related more to the composition of our sample than such extreme scores not being appropriately reflected in the analysis. However, we have followed the reviewer's suggestion and have performed a 'split'-based analysis. As shown in Fig. R1, there is little indication of any reliable difference in the contextual modulation effect for any of the subscales or splits (all independent-samples *t*-tests were not statistically significant).



**Fig. R1.** Comparison of the contextual modulation effects for different participant groups. Participants were allocated into 'high' and 'low' groups based on their relative score on the relevant O-LIFE subscale (different colours), where the criteria for entry into the 'high' and 'low' groups varies as shown on the horizontal axis. The points show the mean difference between the contextual modulation effects (the difference between the threshold with parallel and orthogonal surrounds) in the 'high' and 'low' groups (error bars indicate SEM).

- 4. The question whether the effect addressed in this study, is reliable in schizophrenia needs to be addressed first. Once this question is resolved, then the results presented in this current study can be used independently of the outcome: either as extra evidence that the effect does not exist (no effect) or to report differences in visual perception between patients diagnosed with schizophrenia and individuals with high scoring schizotypy (if there is an effect).**

We agree that further research on the effect in schizophrenia is warranted and important. However, for the reasons enumerated in the response to point #1, we believe that the utility of this study is not entirely conditional on the issue having been resolved in schizophrenia.

## Reviewer #2

- 1. I think that it would be good to assess/report the test-retest reliability of the measures that are correlated, as this limits the power to discover correlations between them.**

The test-retest reliability of the orientation-dependent surround effect cannot be directly assessed in the current data, and we know of no comparable published estimates from similar approaches. However, we can perhaps get an estimate of the reliability of our contrast detection threshold measurement approach by comparing the two orthogonal context conditions. If we assume that the true contrast detection thresholds for a given participant are likely to be very similar in the two orthogonal context conditions (simultaneous and leading surround), we can compare the measured thresholds to get some indication of the reliability (albeit on an overlapping timescale).

As shown in Fig. R2, the contrast detection thresholds are very similar across participants for the two conditions. Though not directly relevant to the reviewer's comment, it may perhaps give some credence to the likelihood of acceptable test-retest reliability for the key measure of interest.

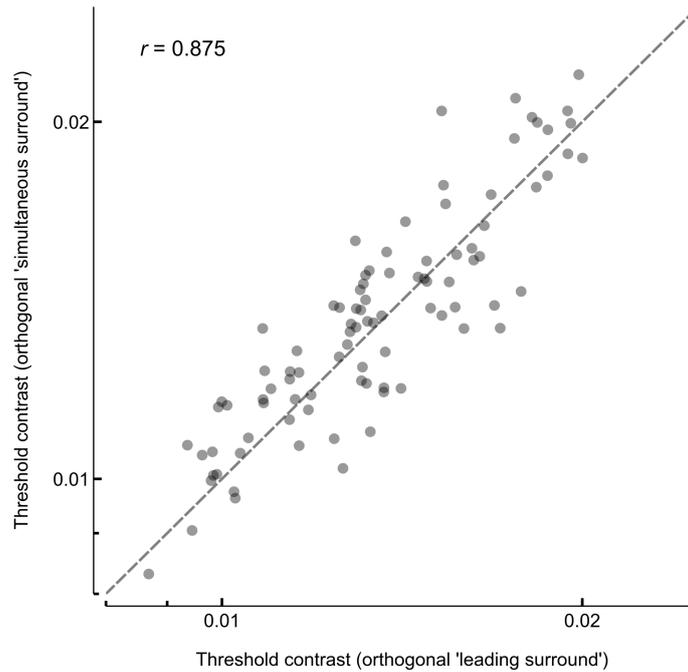
With respect to the O-LIFE, Burch, Steel, & Hemsley (1998) reported test-retest correlations ( $r$ ) of 0.86 for 'unusual experiences', 0.93 for 'cognitive disorganisation', 0.84 for introvertive anhedonia, and 0.77 for 'impulsive nonconformity'. We cite this in the manuscript as describing 'good' test-retest reliability.

- 2. I wonder about the use of sample ranks in describing the correlations in figure 4 and in the statistical significance tests described e.g., on line 199-200. Why are the raw scores not used here? Wouldn't the assumptions of the statistical test for significance of the Pearson correlation coefficient be violated by inducing a near-uniform distribution on the scores? How does this choice affect the analysis in Figure 5? I don't necessarily think that you would find a correlation with the raw scores, but I would have liked to see these scores anyway, because their distribution might shed light on the interpretation of the results.**

The raw scores are not depicted here because we predict a monotonic relationship, rather than a linear relationship, between the O-LIFE scores and the orientation-dependent contextual modulation effect. Hence, we used Spearman's rank correlation method as our measure of association. Given that we wanted to depict the data in a form corresponding to the statistical test, we chose to display the ranked data. We avoided labelling the correlation as Spearman's, as a Pearson's correlation on the ranked data is equivalent to a Spearman's correlation on the raw data.

For completeness, we have added scatterplots comparing the raw scores as Figure S4.

- 3. The discussion concludes with a section that questions whether previous findings in the literature of differences in orientation-selective surround suppression between patients with schizophrenia. In particular, the authors question whether there was an interaction between condition and group in our previous work (Yoon et al. 2009). To allow the authors to assess this interaction, I have made the data publicly available here: <https://github.com/arokem/yoonyoon2009-schizophrenia-bulletin>, and provide an analysis that demonstrates this interaction here: <https://github.com/arokem/yoonyoon2009-schizophrenia-bulletin/blob/master/Yoon2009.ipynb>**



**Fig. R2.** Comparison of contrast detection thresholds for the two orthogonal context conditions. The horizontal and vertical axes (log scales) show the ‘leading’ and ‘simultaneous’ surround conditions, respectively, and each point shows the contrast detection threshold pair for a given participant. The dashed grey line indicates equality between the ‘leading’ and ‘simultaneous’ surround thresholds (it is not a fit to the data). The  $r$  value is the Pearson correlation.

We thank the reviewer for providing access to this raw data. In hindsight, it was possible that a reader would have been left with the implication that the data from this study was not shared with us (rather than us not having sought it)—this was not our intention.

We have updated the relevant section of the Discussion following this analysis:

The fundamental prediction of the proposed alteration of orientation-dependent contextual modulation of contrast perception in schizophrenia is that there will be an interaction between group (those with and without a diagnosis of schizophrenia) and stimulus condition (parallel and orthogonal context orientation) for the relevant dependent variable. In Yoon et al. (2009), the primary dependent variable was the contrast by which a section of a target annulus had to be reduced for participants to perform with 79% accuracy (percent correct) on a yes/no task in which they judged whether there was a section of reduced contrast in the target. While the relevant statistical test for the interaction between group and stimulus condition (parallel and orthogonal surround) was not reported in Yoon et al. (2009), a re-analysis of the data indicated that this interaction is statistically significant ( $F_{1,35} = 5.85$ ,  $p = 0.021$ ). In Serrano-Pedraza et al. (2014), the primary dependent variable was the contrast at which the spatial location of a target could be identified from four alternatives at 62% accuracy (percent correct). The interaction between group and stimulus condition was not statistically significant, providing no evidence for altered orientation-dependent contextual modulation of contrast perception in schizophrenia. Finally, there is also a relevant study by Schallmo et al. (2015) in which the primary dependent variable was the contrast by which an isolated target needed to be adjusted in order to perceptually match the contrast of an adjacent target that was embedded in an articulated spatial context. The interaction

between group (those with and without a diagnosis of schizophrenia) and stimulus condition (parallel and orthogonal surround) was not statistically significant.

The evidence considered thus far for a difference in orientation-dependent contextual modulation of target perception in those with and without a diagnosis of schizophrenia is equivocal—while the data reported in Yoon et al. (2009) show a significant interaction between group (those with and without a diagnosis of schizophrenia) and surround orientation (parallel and orthogonal), the data reported in Serrano-Pedraza et al. (2014) and Schallmo et al. (2015) do not. However, Yoon et al. (2009) and Serrano-Pedraza et al. (2014) also consider a transformed dependent variable in which the performance with parallel and orthogonal context is expressed relative to performance where the target has no articulated surrounding context. In both cases, statistical analysis on such ratios (or log ratios, in Serrano-Pedraza et al. (2014)) demonstrated a significant interaction between group and stimulus condition—with the parallel ratio significantly larger in those without a diagnosis of schizophrenia and the orthogonal ratio not significantly different in those with and without schizophrenia.

- 4. I have also provided the authors with the analysis required in order to assess whether the use of ratios was appropriate in our original paper. I am not entirely sure what to look for here, but it seems that some kind of formal test is required here, as well as in their assessment of the data from Serrano-Pedraza et al.'s work in supplemental Figure 6 (the authors state that “If the assumptions for a valid ratio transform were met, no relationship would be evident in the centre and right columns”, but no formal test of this is presented).**

We again thank the reviewer for providing this data, which allows us to perform a similar analysis of the ratio transformation. We have combined this together with the analysis of the Serrano-Pedraza et al. (2014) data as Article S1.

Briefly, we find that while the data in Yoon et al. (2009) tend to violate the assumption of a zero  $y$ -intercept, the comparisons of the ratios against the no-surround thresholds suggest that this did not have deleterious effects on the interpretation of the ratios.

We have followed the reviewer's request for quantification of the relationship between the ratio and its denominator. Using Spearman's correlation coefficient (we did not necessarily expect this relationship to be linear), we find that there are significant relationships evident in the orthogonal surround conditions in Serrano-Pedraza et al. (2014).

We have updated the relevant section of the Discussion following this analysis:

The nature of the dependent variable thus appears to be relevant to the conclusions drawn about the presence of altered orientation-dependent contextual modulation of contrast perception in schizophrenia. The rationale behind the ratio transformation appears to be based on a desire to adjust for differences in performance in the absence of any articulated context. However, interpreting ratios can be challenging due to a critical requirement to be satisfied in order for the transformation to appropriately achieve the desired control without distortion—specifically, the relationship between the numerator and the denominator must be linear and must pass through the origin (Allison et al. 1995; Curran-Everett 2013). We re-analysed the data of Yoon et al. (2009) and Serrano-Pedraza et al. (2014) to assess these requirements (see Article S1). We find that the requirements were not always satisfied, and that such violations had demonstrable consequences in the Serrano-Pedraza et al. (2014) data while the Yoon et al. (2009) data appeared to be less affected. Hence, we suggest that the comparison between those with and without schizophrenia using such transformed data needs to be interpreted with caution (see Curran-Everett 2013, for further discussion of such issues).

- 5. Furthermore, the presentation of Schallmo et al.'s results in this section makes it seem as though they found no difference between controls and patients, where such a difference was found, using a normalized contextual modulation index. Was use of this normalized index justified in that case?**

This section was concerned with the interaction between group (patient and control) and surround orientation (parallel and orthogonal). We are not sure which result the reviewer is referring to here—Schallmo et al. (2015) did not find a difference between parallel and orthogonal surround orientation conditions (their ‘normalized contextual modulation index’) between controls and patients (“These results indicate that different surround configurations evoked similar changes in contrast perception across all subject groups”, p. 3531). Furthermore, the indices used by Schallmo et al. (2015) were differences and are hence not related to the other discussions around ratios.

- 6. Another interpretation of these results is that the personality measure of schizotypy does not capture the biological variability that is captured by orientation-selective surround suppression, and that OSSS taps some other critical biological factors that distinguish high-schizotypy individuals from those that develop schizophrenia symptoms (this is also mentioned in the Ettinger review cited). I think that it would be appropriate to present this alternative interpretation as well.**

We believe that this interpretation is covered in the following section of the Discussion:

The results of the current study are consistent with psychometrically-defined schizotypy being unrelated to the orientation-dependent modulation of visual contrast detection. Given that previous studies report that the extent of such orientation-dependent contextual modulation is related to a diagnosis of schizophrenia (Serrano-Pedraza et al. 2014; Yoon et al. 2009), this suggests that orientation-dependent modulation of visual contrast detection may be a situation in which schizophrenia and psychometrically-defined schizotypy are dissociated. As stated by Ettinger et al. (2015), such situations can be indicative of “protective or compensatory mechanisms” (p. S418) and are hence of considerable interest in understanding the transition to psychosis. Orientation-dependent contextual modulation may be a particularly useful paradigm for revealing such mechanisms due to its well-studied behavioural and neural foundations (Seymour et al. 2013; Yoon et al. 2013) and established theories regarding its circuitry in schizophrenia (Yoon et al. 2010). Should the results and conclusions presented here prove to be robust, future studies using schizotypy may usefully correspond and interact with investigations of schizophrenia to aid in clarifying the mechanisms that selectively relate to the transition to disorder.

- 7. The link to Bitbucket on L88 is broken because of the line-break, and reflow with L89.**

This appears to be introduced in the compilation process and would presumably not affect final typesetting—thanks for pointing it out and we will be sure to check it (if the manuscript should advance to production).

- 8. How occasionally were items unanswered?**

We have added this information to the manuscript as follows:

Items on the O-LIFE questionnaire were occasionally either unanswered (1 response), answered with both response options (2 responses across 1 participant), or ambiguously answered (3 responses across 3 participants)—such items were replaced with the modal value from that subscale for that participant, after any negative scoring.

- 9. typo: “an” => “a”**

Thanks—corrected.

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