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Reproducibility of leftward planum temporale asymmetries in two genetically isolated populations of chimpanzees (*Pan troglodytes*)

Muhammad A. Spocter, Chet C. Sherwood, Steven J. Schapiro and William D. Hopkins

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1st revised submission:	4 August 2020
2nd revised submission:	17 August 2020
Final acceptance:	17 August 2020

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

Review History

RSPB-2020-1320.R0 (Original submission)

Review form: Reviewer 1

Recommendation
Major revision is needed (please make suggestions 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

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

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

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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
Please see attached file (See Appendix A).

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

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

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Is it accessible?
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Is it clear?
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Is it adequate?
Yes

Do you have any ethical concerns with this paper?
No

Comments to the Author
Spocter et al. have submitted an impressive data set on PT-asymmetries and its heritability in chimps. These results show how similar chimp and human asymmetries of the temporal lobe are. In addition, they demonstrate that rearing conditions play no major role. Overall, this is an important study and I have only minor requests.

The authors list previous publications on the relationship between PT- and language-asymmetry in humans but mainly refer to studies on gross morphology. To convince the reader that a larger PT-surface (or volume) also goes along with differences in internal morphology and language-related physiology, a few remarks into this direction could be useful (e.g. Galuske et al., Science, 2000; Ocklenburg et al., Science Adv., 2018).

All together, these studies, however, create a logical conundrum since chimps don't speak. Space is restricted in Proceedings B, but could the authors nevertheless insert a few speculations why we see morphological asymmetries similar to the human language condition in the brain of a chimp? This could set, however speculative, an evolutionary framework for the reader.

Where the animals anesthetized during MR. How?

Decision letter (RSPB-2020-1320.R0)

15-Jul-2020

Dear Dr Spocter:

Your manuscript has now been peer reviewed and the reviews have been assessed by two reviewers and an Associate Editor. All of us think your manuscript has the potential to be quite important, however the reviewers have indicated several concerns that need to be addressed. In particular, Reviewer 1 makes some excellent points about organization and presentation, and I agree with reviewer 2's suggestion that you provide more speculation about how this relates to the evolution of language. 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. Please pay careful attention to each of their suggestions as you revise your manuscript.

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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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,
Dr Sarah Brosnan
Editor, Proceedings B
mailto: proceedingsb@royalsociety.org

Associate Editor
Board Member: 1
Comments to Author:
We have now heard from two experts in the field. Although both reviewers were positive about your manuscript, they have raised some concerns that will need your attention. Reviewer 1, in particular points, to several places in the manuscript where you need to be clearer about what you mean. I suggest that you read the comments carefully. Some reorganization of the Results and/or the Discussion might be required -- and some of the language around genetics needs to be clarified.

Reviewer(s)' Comments to Author:
Referee: 1

Comments to the Author(s)
Please see attached file.

Referee: 2

Comments to the Author(s)
Spocter et al. have submitted an impressive data set on PT-asymmetries and its heritability in chimps. These results show how similar chimp and human asymmetries of the temporal lobe are. In addition, they demonstrate that rearing conditions play no major role. Overall, this is an important study and I have only minor requests.

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Where the animals anesthetized during MR. How?

Author's Response to Decision Letter for (RSPB-2020-1320.R0)

See Appendix B.

Decision letter (RSPB-2020-1320.R1)

17-Aug-2020

Dear Dr Spocter

I am pleased to inform you that your Review manuscript RSPB-2020-1320.R1 entitled "Reproducibility of Leftward Planum Temporale Asymmetries in Two Genetically Isolated Populations of Chimpanzees (Pan troglodytes)" has been accepted for publication in Proceedings B.

The referee(s) do not recommend any further changes. Therefore, please proof-read your manuscript carefully and upload your final files for publication. Because the schedule for publication is very tight, it is a condition of publication that you submit the revised version of your manuscript within 7 days. If you do not think you will be able to meet this date please let me know immediately.

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3) Electronic supplementary material: this should be contained in a separate file from the main text and the file name should contain the author's name and journal name, e.g authorname_procb_ESM_figures.pdf
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Once again, thank you for submitting your manuscript to Proceedings B and I look forward to receiving your final version. If you have any questions at all, please do not hesitate to get in touch.

Sincerely,
Dr Sarah Brosnan
Editor, Proceedings B
mailto:proceedingsb@royalsociety.org

Associate Editor Board Member
Comments to Author:
I have now read through your revised manuscript. Thank you for paying close attention to the comments of the reviewers. You have dealt with their queries and suggestions admirably. Congratulations on a fine piece of work.

Please add a link to your data in the Data Accessibility section.

Decision letter (RSPB-2020-1320.R2)

17-Aug-2020

Dear Dr Spocter

I am pleased to inform you that your manuscript entitled "Reproducibility of Leftward Planum Temporale Asymmetries in Two Genetically Isolated Populations of Chimpanzees (Pan troglodytes)" 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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Appendix A

Reproducibility of Leftward Planum Temporale Asymmetries in Two Genetically Isolated Populations of Chimpanzees (Pan troglodytes) (RSPB-2020-1320)

This is an interesting manuscript in which the authors report the application of an image analysis pipeline developed using BrainVISA software to measure the surface area and depth of the planum temporale (PT). 3D MRI scans of the brain obtained for a large cohort of 291 chimpanzees (165 females and 126 males, aged between 3 to 52 years) from two captive populations (155 at the University of Texas (NCCC) and 136 at Yerkes National Primate Research Center (YNPRC)) that are described as genetically isolated from each other. The 3D images were obtained in-vivo for 229 chimpanzees using either a 3 T or 1.5 T MRI system and post mortem for 62 chimpanzees using either a 4.7 or 7 T MRI system. A Heritability analysis was also performed using SOLAR software together with an analysis of the potential effect of whether the chimpanzees were mother reared, nursery reared or wild caught. For the entire cohort, significant leftward asymmetry of the suface area and depth of the PT was observed. Furthermore, heritability of leftward asymmetry of the surface area and depth of the PT was observed. The authors conclude that leftward bias of PT asymmetry in chimpanzees is confirmed and that genetic mechanisms play a key role in the emergence of asymmetry in this brain region.

The following points should be addressed.

1. From the outset the authors frequently refer to PT asymmetry without specifying the measurement that is asymmetric, and which could be volume, surface area, depth, shape or cortical thickness. The units of the measurement should be clarified for the present study (e.g. in Abstract) and when referring to published studies in the Introduction and Discussion. The significance of the different types of measurement should also be discussed.

2. In the penultimate paragraph of the Introduction the authors state that one goal of the study was to examine heritability of asymmetries in the PT. In particular, they state that they will evaluate the ***reproducibility*** of (1) phenotypic asymmetries and (2) their potential genetic foundations. In the next paragraph they go on to say that they will investigate the ***repeatability*** of PT asymmetries in respect of (1) field strength of the MRI system, (2) sex, (3) handedness and (4) rearing history. The Results section however has an alternative, somewhat reversed, structure in which firstly "Descriptive Data on PT asymmetry", and which includes a multivariate analysis of covariance of population groups, rearing groups and sexes, are presented and secondly a "Heritability Analysis". Finally, in the concluding paragraph of the Discussion a different structure again is used with a different (1), (2) and (3). A rather modest reorganisation, together with definition of reproducibility and repeatability, could potentially greatly assist the reader to follow the interesting findings that are reported. Also, appropriate mention of comparison of in-vivo and post mortem imaging should be included.

3. Clarification should be given regarding what exactly is being referred to in Figure 3 in the second and third paragraphs of the Results section.

4. All of the measurements are reduced to being used in an analysis of asymmetry. I recommend that the raw data should also be plotted in Figure 3. In particular, it would be interesting to know whether there is a systematic difference between the values of PT surface area and depth in the left and right cerebral hemispheres obtained for the images acquired in-vivo and post mortem, and the variation in these quantities with respect to age, sex, rearing and field strength.

5. In the Results section clarification should also be given in respect of the somewhat different findings obtained from the Heritability analysis in the NCCC and YNPRC groups. In particular, the sentence beginning "In sum …" is difficult to follow.

6. The authors report that PT surface area asymmetry, but not PT depth asymmetry, is heritable. What information does this provide regarding the nature of the asymmetry (see also [1] above regarding the different types of measurement).

7. The 3D MR images are of the whole brain and the BrainVISA pipeline could be adapted to measure all brain structures. However, it is an important that the study is entirely focussed on the analysis of the PT. Accordingly, remarks such as that brain asymmetry is widely shared between humans and other animals should be clarified. Whilst there was already convincing evidence, now supported by the present study, that PT asymmetry is shared between humans and chimpanzees, this may not be the case with other primates. Furthermore, particular brain asymmetries (e.g. the torque) may be human specific (Li et al., 2018). Hou et al. (2019) have reported that a significant relationship exists between the cerebral torque and Sylvian Fissure asymmetry in humans but not in chimpanzees. The PT is contained within the Sylvian Fissure and it is important to consider the relationship between local and global brain asymmetries.

8. A fuller description of what is mean by "genetically isolated" (see page 3) populations and "the genetic correlation" (see page 14) would be helpful. Which genes are being referred to?

9. On page 3 it is stated that "In humans, PT asymmetry is associated with severe deficits in language comprehension and production …". Is this a suggestion that PT asymmetry is associated with a potential deficit in cognition in humans and/or chimpanzees or that PT asymmetry is related to language?

Reference

Hou L, Xiang L, Crow TJ, Leroy F, Rivière D, Mangin JF, Roberts N. Measurement of Sylvian Fissure asymmetry and occipital bending in humans and Pan troglodytes. Neuroimage, 184, 855-870 (2019.

Appendix B

Dear Professor Sara Brosnan,

Thank you for the consideration of our submission entitled " Reproducibility of Leftward Planum Temporale Asymmetries in Two Genetically Isolated Populations of Chimpanzees (*Pan troglodytes*)" (RSPB-2020-1320) and for sharing with us the referees' reviews. We appreciate the thoughtful comments and have taken these into consideration and made changes as requested. These changes are reflected in the revised manuscript (track changes) and also outlined below to facilitate review of this revision. We thank you for helping to improve the quality of the manuscript.

Thank you for your consideration of this revised submission.

Muhammad

Muhammad. A. Spocter, Ph.D.
Associate Professor
Department of Anatomy
Des Moines University
3200 Grand Avenue
Iowa, 50312

With reference to the comments made by Referee 1:

1. ***From the outset the authors frequently refer to PT asymmetry without specifying the measurement that is asymmetric, and which could be volume, surface area, depth, shape or cortical thickness. The units of the measurement should be clarified for the present study (e.g. in Abstract) and when referring to published studies in the Introduction and Discussion. The significance of the different types of measurement should also be discussed.***

   We have updated the manuscript to clarify throughout the text references to measurement of PT asymmetry. In the abstract (lines 47-51) we have added the following to clarify the measure of interest:

   Using magnetic resonance imaging (MRI) we evaluated morphological asymmetries of PT surface area (mm^2) and mean depth (mm) in captive chimpanzees (N = 291) derived from two genetically isolated populations. Our results confirm that chimpanzees exhibit a significant population-level leftward asymmetry for PT surface area, as well as significant heritability in the surface area and mean depth of the PT.

   Under the Methods sub section Sulci Extraction and Measurement, we also updated the manuscript to include the measurement units for PT surface area (mm^2), and mean sulcal depth (mm) (lines 202 -203 and line 213).

We have included the following statement on the significance of the different types of measurement used in the current study (lines 129-150).

In particular, the surface area of the PT is on average larger in the left hemisphere, which is significant in that it overlaps with Wernicke's area, a key brain region involved in auditory and lexical processing which is associated with functional cerebral lateralization for language. In humans, deviations from normal PT asymmetry are associated with severe deficits in language comprehension and production (Borovsky, Saygin, Bates, & Dronkers, 2007; Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004; Foundas et al., 2004; Geschwind & Levitsky, 1968; Wernicke, 1874). In addition, comparisons of sulcal depth in regions surrounding the PT, have also proven useful as markers of neurological dysfunction (e.g., Csernansky et al., 2008; Ilwoo et al., 2018) as well as species-specific morphology (Leroy et al., 2015), prompting further exploration of PT asymmetry and its functional implications (Ocklenburg et al., 2018; Josse, Kherif, Flandin, Seghier, & Price, 2009; Josse, Mazoyer, Crivello, & Tzourio-Mazoyer, 2003)

Ilwoo, L., Kang, H., Woodward, N.D., & Landman, B.A (2018). Sulcal depth-based cortical shape analysis in normal healthy control and Schizophrenia groups. Proc SPIE Int. Soc Opt Eng, 10574, 1057402.

Csernansky, J.G., Gillespie, S.K., Dierker, D.L., Anticevic, A., Wang, L., Barch, D.M., & Van Essen, D.C. (2008). Symmetric abnormalities in sulcal patterning in schizophrenia. Neuroimage, 43 (3), 440-446.

François Leroy, Qing Cai, Stephanie L. Bogart, Jessica Dubois, Olivier Coulon, Karla Monzalvo, Clara Fischer, Hervé Glasel, Lise Van der Haegen, Audrey Bénézit, Ching-Po Lin, David N. Kennedy, Aya S. Ihara, Lucie Hertz-Pannier, Marie-Laure Moutard, Cyril Poupon, Marc Brysbaert, Neil Roberts, William D. Hopkins, Jean-François Mangin, Ghislaine Dehaene-Lambertz (2015). New human-specific brain landmark: The depth asymmetry of superior temporal sulcus. Proceedings of the National Academy of Sciences Jan 2015, 112 (4) 1208-1213; DOI: 10.1073/pnas.1412389112

2. ***In the penultimate paragraph of the Introduction the authors state that one goal of the study was to examine heritability of asymmetries in the PT. In particular, they state that they will evaluate the reproducibility of (1) phenotypic asymmetries and (2) their potential genetic foundations. In the next paragraph they go on to say that they will investigate the repeatability of PT asymmetries in respect of (1) field strength of the MRI system, (2) sex, (3) handedness and (4) rearing history. The Results section however has an alternative, somewhat reversed, structure in which firstly "Descriptive Data on PT asymmetry", and which includes a multivariate analysis of covariance of population groups, rearing groups and sexes, are presented and secondly a "Heritability Analysis". Finally, in the concluding paragraph of the Discussion a different structure again is used with a different (1), (2) and (3). A rather modest reorganisation, together with definition of reproducibility and repeatability, could potentially***

greatly assist the reader to follow the interesting findings that are reported. Also, appropriate mention of comparison of in-vivo and postmortem imaging should be included.

We have reorganized the manuscript so that the introduction is consistency with the sequence with which the results are reported and made similar changes to the subsequent discussion section. The penultimate paragraph in the Introduction now reads (line 207-234):

To this end, we examined the repeatability and heritability of asymmetries in the PT of common chimpanzees. Specifically, in vivo and postmortem magnetic resonance imaging (MRI) scans were obtained from two captive chimpanzee populations that are genetically isolated from each other (i.e., the two populations are geographically isolated from one another and there is no gene flow between the two groups), but for whom there are well-documented pedigrees dating back to the founder animals (Hopkins, Mareno, & Schapiro, 2019). By measuring PT surface area (mm^2) and the mean sulcal depth (mm) in these two populations, we had a unique opportunity to evaluate the consistency with which PT phenotypic asymmetries could be observed across a variety of non-genetic factors including MRI scanner magnet strength, sex, handedness, and rearing history. For example, some have suggested that population-level behavioral asymmetries in nonhuman primates, including chimpanzees, may be influenced by their early handling by right-handed humans (McGrew & Marchant, 1997). In rodents, there is good evidence that early handling can induce population-level behavioral asymmetries (Denenberg & Yutzey, 1985). Within our sample, we had chimpanzee subjects with differing early social rearing experiences with human caregivers, and this allowed us to test this hypothesis as it relates to PT asymmetries. If early handling experiences by human's influence PT asymmetries, then we hypothesized that apes with more extensive caregiver contact would differ from chimpanzees with less history of human handling. Furthermore, through the use of heritability analyses we explored the proportion of variance in PT asymmetry in chimpanzees associated with genetic factors. We hypothesized that if population-level PT asymmetries are reproducible across chimpanzee populations and under genetic control, then significant leftward biases and heritability would be evident in the surface area and or sulcal depth of the PT in both cohorts.

Minor adjustments to the Results section were also made to keep the sequence with which these results were reported consistent (see line 351-354 and line 362)

Minor adjustments to the Discussion section were also made. The concluding paragraph in the Discussion now reads (line 533-545):

In conclusion, the present study provides important confirmatory data that the leftward asymmetries in the PT of chimpanzees is robust and is evident across two distinct genetically isolated populations. Further, leftward asymmetries in the PT were consistently found across two cohorts studied and were found to be independent of the (1) MRI magnet strength and scanning protocol, (2) the sex of the individual, and (3) early

social rearing experiences. Surface area and mean depth of the PT were significantly heritable, and these patterns of results were largely consistent between the two chimpanzee populations. The collective findings suggest that asymmetries in the PT have a strong biological basis, and that this evolutionary foundation was likely evident in the last common ancestor of chimpanzees and humans, serving as a pe-adaptation for modern human language and speech (Hopkins et al., 2007). The presence of PT asymmetries in the last common ancestor may have set the stage for the emergence of lateralization to the left hemisphere in language functions in modern humans.

3. ***Clarification should be given regarding what exactly is being referred to in Figure 3 in the second and third paragraphs of the Results section.***

   We have clarified the reporting of Figure 3. Paragraph two of the results section (line 350-354) now reads:

For descriptive purposes, we also report the percentage of chimpanzees that were classified as having a left, right or no bias (based on the AQ cut points) in PT surface area and mean depth asymmetry (see Figure 3 A & B and table S3). For each measure, the percentage of chimpanzees classified left, right and no bias in PT asymmetry is shown across scanner magnet strength, rearing history, sex and chimpanzee colony.

4. ***All of the measurements are reduced to being used in an analysis of asymmetry. I recommend that the raw data should also be plotted in Figure 3. In particular, it would be interesting to know whether there is a systematic difference between the values of PT surface area and depth in the left and right cerebral hemispheres obtained for the images acquired in-vivo and post mortem, and the variation in these quantities with respect to age, sex, rearing and field strength.***

   We have added a Table S3 that includes the means and standard errors for the left and right hemisphere PT surface area and mean depth values between chimpanzees (1) scanned with different magnets (2) for males and females (3) for the NCCC and YNPC colonies and (4) between the MR, NR and WC reared apes.

5. ***In the Results section clarification should also be given in respect of the somewhat different findings obtained from the Heritability analysis in the NCCC and YNPRC groups. In particular, the sentence beginning "In sum …" is difficult to follow.***

We have made adjustments to the Results section (line 378-418).

Heritability in the left and right hemisphere PT surface areas and mean depths were determined for the entire sample. Scanner magnet strength, sex, age and colony were used as covariates. We found significant heritability in the mean hemisphere PT

surface area (h^2 =0.22; p < .05) as well as the mean sulcal depth of the PT (h^2 range =0.42; p < .05). Detailed results from these analyses are provided in the electronic supplementary material, table S2. Additionally, we found a small, but significant, heritability for the AQ surface area (h^2 =0.13; p < .05), but not the mean depth AQ (h^2 =0.03; p > .05). We also estimated heritability within the NCCC and YNPRC populations separately to examine consistency in heritability between the two populations. Within the NCCC population, significant heritability was found for both mean PT surface area and mean depth. In contrast, for the YNPRC population we failed to find significant heritability in mean PT surface area, although the mean depth, was significantly heritable. Thus, heritability in the mean depth of the PT was consistently significant between the NCCC and YNPRC chimpanzee populations. In contrast, heritability in surface area was not found to consistently be significant between the NCCC and YNPRC populations. Lastly, we performed genetic correlations between the left and right hemisphere surface area and mean depth values for the entire chimpanzee sample. A significant genetic correlation was found for mean depth (rhoG = .975, s.e. = .189 p < .001), but not for surface area, though the estimate approached conventional levels of statistical significance (rhoG =.755, s.e. = .212, p < .054).

6. ***The authors report that PT surface area asymmetry, but not PT depth asymmetry, is heritable. What information does this provide regarding the nature of the asymmetry (see also [1] above regarding the different types of measurement).***

We have added a note regarding this point to the Discussion section (line 424-430). This reads:

Lastly, we found a small but significant heritability in the AQ scores for the PT mean depth but no the surface area. These findings are difficult to interpret in light of the inconsistency in findings between the measures and the relatively small effect size. In our view, these results should be viewed with some caution. Arguably, perhaps molecular biological methods might produce more compelling evidence for genetic factors influencing directional asymmetries than quantitative genetic approaches.

7. ***The 3D MR images are of the whole brain and the BrainVISA pipeline could be adapted to measure all brain structures. However, it is an important that the study is entirely focussed on the analysis of the PT. Accordingly, remarks such as that brain asymmetry is widely shared between humans and other animals should be clarified. Whilst there was already convincing evidence, now supported by the present study, that PT asymmetry is shared between humans and chimpanzees, this may not be the case with other primates. Furthermore, particular brain asymmetries (e.g. the torque) may be human specific (Li et al., 2018). Hou et al. (2019) have reported that a significant relationship exists between the cerebral torque and Sylvian Fissure asymmetry in humans but not in chimpanzees. The PT is contained within the Sylvian Fissure and it is***

important to consider the relationship between local and global brain asymmetries.

In accordance with the Referees suggestion, we have made adjustments throughout the text to indicate that this study is specifically focused on asymmetry in the planum temporale and does not address asymmetry in general.

We feel the results from the current study add further evidence in support of the continuity in form between humans and other species. Although the exact nature (i.e., global or regional differences) and degree of asymmetry might vary greatly between the humans and other species, these results emphasize that brain asymmetry is not a uniquely human feature and that many mammalian brains have some form of asymmetry.

8. ***A fuller description of what is mean by "genetically isolated" (see page 3) populations and "the genetic correlation" (see page 14) would be helpful. Which genes are being referred to?***

This has been clarified in the text (line 138-142)

Specifically, in vivo and postmortem magnetic resonance imaging (MRI) scans were obtained from two captive chimpanzee populations that are genetically isolated from each other (i.e., the two populations are geographically isolated from one another and there is no gene flow between the two groups), but for whom there are well-documented pedigrees dating back to the founder animals (Hopkins, Mareno, & Schapiro, 2019).

By genetically isolated, we are describing the fact that the YNPRC and NCCC populations each were started with different founder animals. Furthermore, there was no interbreeding between the sires and dams between the two colonies. Thus, there are no related individuals between the YNPRC and NCCC chimpanzees. Imagine you had a sample of chimpanzees and formed two groups of males and females and placed one group on an island in the Pacific and one on an island in the Atlantic Ocean. You left them there and let them breed for > 50 years, then compared their brain phenotypes.

Regarding genetic correlations, they refer to the proportion of variance between two traits that are due to shared genetic factor. Genetic correlation at or near zero suggest that the genes that potentially influence Trait #1 are entirely independent of those that influence Trait #2. In contrast, for high genetic correlations, the inference is that the same potential genes that influence Trait #1 also influence Trait #2.

9. ***On page 3 it is stated that "In humans, PT asymmetry is associated with severe deficits in language comprehension and production …". Is this a suggestion that PT asymmetry is associated with a potential deficit in cognition in humans and/or chimpanzees or that PT asymmetry is related to language?***

   We have clarified this to read (lines 132-133):

   In humans, deviations from normal PT asymmetry are associated with severe deficits in language comprehension and production (Borovsky, Saygin, Bates, & Dronkers, 2007; Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004; Foundas et al., 2004; Geschwind & Levitsky, 1968; Wernicke, 1874).

10. ***Hou L, Xiang L, Crow TJ, Leroy F, Rivière D, Mangin JF, Roberts N. Measurement of Sylvian Fissure asymmetry and occipital bending in humans and Pan troglodytes. Neuroimage, 184, 855-870 (2019).***

    We thank the Referee for this suggestion and have included this in the text.

<u>With reference to the comments made by Referee 2:</u>

1) ***The authors list previous publications on the relationship between PT- and language-asymmetry in humans but mainly refer to studies on gross morphology. To convince the reader that a larger PT-surface (or volume) also goes along with differences in internal morphology and language-related physiology, a few remarks into this direction could be useful (e.g. Galuske et al., Science, 2000; Ocklenburg et al., Science Adv., 2018).***

   We thank the Referee for these valuable citations and have included this in the text.

   In addition, comparisons of sulcal depth in regions surrounding the PT, have also proven useful as markers of neurological dysfunction (e.g., Csernansky et al., 2008; Ilwoo et al., 2018) as well as species-specific morphology (Leroy et al., 2015), prompting further exploration of PT asymmetry and its functional implications (Ocklenburg et al., 2018; Josse, Kherif, Flandin, Seghier, & Price, 2009; Josse, Mazoyer, Crivello, & Tzourio-Mazoyer, 2003).

   2) All together, these studies, however, create a logical conundrum since chimps don't speak. Space is restricted in Proceedings B, but could the authors nevertheless insert a few speculations why we see morphological asymmetries similar to the human language condition in the brain of a chimp? This could set, however speculative, an evolutionary framework for the reader.

We thank the Referee for this suggestion and have included the following few lines to the text (lines 540-545).

The collective findings suggest that asymmetries in the PT have a strong biological basis, and that this evolutionary foundation was likely evident in the last common ancestor of chimpanzees and humans, serving as a pe-adaptation for modern human language and speech (Hopkins et al., 2007). The presence of PT asymmetries in the last common ancestor may have set the stage for the emergence of lateralization to the left hemisphere in language functions in modern humans.

3) Where the animals anesthetized during MR. How?

We have included the following few lines into the Electronic Supplemental Materials to clarify the procedure.:

In vivo scans were obtained at the time the chimpanzees were being surveyed for their annual physical examinations. All in vivo chimpanzee MRI scans were done prior to the 2015 implementation of United States Fish and Wildlife Service and National Institutes of Health regulations governing research with chimpanzees. Subjects were first immobilized with ketamine (10 mg/kg) or telazol (3-5mg/kg) and subsequently anaesthetized with propofol (40–60 mg/(kg/h)), following standard procedures at the YNPRC and NCCC facilities. YNPRC subjects were then transported to the MRI facility, while NCCC subjects were wheeled to the mobile imaging unit.