

Peer Review Overview

Manuscript Title: Electrophysiological differences and similarities in audiovisual speech processing in CI users with unilateral and bilateral hearing loss



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1st Decision letter

Reference: CRNEUR-D-22-00040

Title: Electrophysiological differences and similarities in audiovisual speech processing in CI users with unilateral and bilateral hearing loss

Journal: Current Research in Neurobiology

Dear Mrs. Layer,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following revision. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by Sep 11, 2022.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully; outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission will need to be re-reviewed.

Current Research in Neurobiology values your contribution and I look forward to receiving your revised manuscript.

CRNEUR aims to be a unique, community-led journal, as highlighted in the [Editorial Introduction](#). As part of this vision, we will be regularly seeking input from the scientific community. We encourage you and your co-authors to take the [survey](#) as part of the editorial.

Kind regards,

Kerry Walker, DPhil
Associate Editor
Current Research in Neurobiology

Comments from Editors and Reviewers:

Editor: Both reviewers agree that there is scientific merit in this manuscript, but that it would benefit from some improvements. In particular, the authors should improve their use of multiple statistical tests to answer the most relevant research questions. The reviewers have also requested clarifications to the presentation and discussion of the results in this paper, and how they relate to the existing literature. We look forward to considering the author's revised manuscript.

Reviewer #1:

The manuscript entitled "Electrophysiological differences in audiovisual speech processing in CI users with unilateral and bilateral hearing loss" by Layer and colleagues investigates the experience-dependent impact of atypical hearing on auditory and multisensory processing. To this end syllables (in A, V and AV conditions) were presented while the EEG was recorded in three groups of participants hearing controls, CI users with unilateral or bilateral hearing loss. The study represents an expansion of a previous study from the same group (Layer et al., 2022) in which the data of hearing controls and of CI with bilateral hearing loss were presented.

The rationale is clear and results are very interesting. In particular they reveal unique effects of adaptation in the group of CI with bilateral hearing loss compared to unilateral hearing loss (stronger visual impact on auditory processing) as well as common effects associated with implantation (e.g. delayed N1).

Major comments

1) While I find the work of extreme relevance and interest, it is opinion of the present reviewer that the authors are conducting an extensive number of statistical tests, though with different approaches, on the same data. I am wondering whether, a reduction of the number of analyses and a detailed definition of the hypothesis on investigated factors would improve the clarity of the work without compromising the conveyed messages.

As an example:

"The GFP peak mean amplitudes and latencies were detected for each individual, condition (A, AV-V) and time window (N1, P2) and were statistically analysed by using a 3 x 2 mixed ANOVA with group (NH, CI-CHD, CI-SSD) as the between-subjects factor and condition (A, AV-V) as the within-subjects factor for each peak separately."

The authors analyzed separately Latency, Amplitude of N1 and P2 waves resulting in four different ANOVAs. I wonder, is there any specific reason why not including wave (N1 or P2) as factors? I counted at 4 ANOVAs on the GDP, 2 ANOVAs on Hierarchical clustering and single-subject fitting analysis, and 4 ANOVAs on source modeling. Corrections are performed for multiple t-tests, but no corrections are performed across the ANOVAs. While I am not specifically asking to implement correction for the number of ANOVAs, I would suggest taking into consideration the approach by Cramer et al. 2016 where family wise or false discovery rate corrections are suggested in addition to providing detailed hypothesis on the factors investigated.

2) I wonder whether the authors should acknowledge (discussion) the possibility that the observed effects could emerge with other types of A-V stimuli and not necessarily pertain to language processing.

3) Figures. ERPs and source timeseries of the data in the source domain would benefit from having SE included as shaded region.

4) It would be relevant to have access to the stimuli

Reviewer #2:

The authors present a study that is follow up to a previously published paper. The only thing that appears to be really different in this study is the addition of an SSD group (the comparison data is identical to the previously published data). I will leave it to the editor to determine if this in itself is worthy of a separate publication.

The methods are sound.

Comments:

The biggest effect is that of the P2. In the auditory condition, there is a large P2 response for the auditory condition. The authors only report the AV-V condition. This is pretty annoying and I would have liked to have seen the all three conditions overlaid. I understand that the authors are comparing additive effects models, but, nonetheless, having see the raw data for visual only would be nicer and give a more complete picture.

What is contributing to the P2? What is the dominant generator? (aside from the ROIs listed)

How do these data correlate to speech perception?

I would like to see some more discussion of the differences between SSD and CHD. This is really the whole point of the paper!

1st Author Response Letter

Response to comments from Editors and Reviewers:

Dear Prof. Walker and Prof. Petkov,
Dear Reviewers,

We thank the Reviewers for their helpful comments on the manuscript. The manuscript has been revised on the basis of the Reviewers' comments, which helped us to further improve the quality of the manuscript.

We are uploading our point-by-point response to the comments and an updated manuscript in which the changes to the former version of the manuscript are highlighted in red. Following the suggestions of the reviewers, we added supplementary material to the manuscript, including the GFP and GMD data of the other conditions (V, AV) and we uploaded the video files of the stimuli to make them freely available.

Comments from Reviewer 1

The manuscript entitled "Electrophysiological differences in audiovisual speech processing in CI users with unilateral and bilateral hearing loss" by Layer and colleagues investigates the experience-dependent impact of atypical hearing on auditory and multisensory processing. To this end syllables (in A, V and AV conditions) were presented while the EEG was recorded in three groups of participants hearing controls, CI users with unilateral or bilateral hearing loss. The study represents an expansion of a previous study from the same group (Layer et al., 2022) in which the data of hearing controls and of CI with bilateral hearing loss were presented.

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Comment 1:

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Response to comment 1:

Thank you for recommending the paper of Cramer et al. (2016), which indeed includes useful guidelines for improving the statistical validity in studies. We carefully consider this point, although we would like to emphasise that the various dependent measures we analysed are distinct, and in some cases they are even independent of one another. For instance, GFP and GMD are independent variables. In addition, some of the dependent measures are univariate and others are multivariate. Single subject fitting is similar to the GMD but is not the same dependent measure being analysed. Due to these reasons, we do

not share the view that many of our analyses are performed on the same data. Nevertheless, we agree that it is critical to have clear hypotheses in mind to justify the various ANOVAs. In addition, it is important to clearly communicate that this is a small sample and that the results must be interpreted with caution. To address this issue, we added a limitations section (page 31, line 1108-1118) and some more sentences in the manuscript:

- 1) *Introduction: page 4, line 131-136: "This is noteworthy because literature comparing CI-SSD to bimodal or bilateral CI users is scarce. However, the few existing studies reported differences in speech-in-noise performance (Williges et al., 2019) and in situations with multiple concurrent speakers (Bernstein et al., 2016) between CI-SSD users and bimodal or bilateral CI users, respectively. But, given this first evidence for purely auditory situations, we hypothesised that further differences would emerge for audiovisual stimulation, which has yet to be reported."*
- 2) *Discussion: page 28, line 965-974: "Previous research comparing different groups of CI users is limited. Nevertheless, first evidence of differences in speech-in-noise performance between CI-SSD users and bimodal CI users (CI on one ear and hearing aid on the contralateral ear) was reported (Williges et al., 2019). On the other hand, differences between CI-SSD users and bilateral CI users (both ears fitted with CIs) were observed in situations with multiple concurrent speakers (Bernstein et al., 2016). As a result, we expected group differences to emerge not only for auditory stimulation but also for audiovisual stimulation. However, as far as we are aware, this has not been investigated yet. Our results therefore indeed confirm first indications of different processing strategies among different CI user groups."*

Concerning the question of why we did not analyse the N1 and P2 within the same ANOVA, we simply followed the procedure of nearly all previous similar studies (e.g. Bottari et al., 2014 *NeuroImage*; Soshi et al., 2014 *Hearing Research*). Moreover, we had no hypotheses regarding potential interaction effects between the N1 and the P2 ERPs, and Cramer et al. (2016) pointed out that the inclusion of many factors results in a higher alpha error probability. Therefore, we refrained from computing (supplementary) ANOVAs containing the N1 and P2 ERP parameters within the same analysis.

We acknowledge the important comment from the Reviewer, as we agree that some of our hypotheses may not have been specified clearly enough. Therefore, we followed the recommendations of Cramer et al. (2016) by more explicitly mentioning the hypotheses that are mainly based on our previous results (Layer et al., 2022). The hypotheses on our data are now described in detail in various parts of the manuscript.

In the introduction, we broadly state our hypotheses:

"Given that CI-SSD users have an intact ear on the contralateral side, it is reasonable that this NH ear serves as the main communication channel despite the advantages given by the CI (Kitterick et al., 2015; Ludwig et al., 2021). Therefore, we hypothesised that CI-SSD users are less influenced by visual information, benefit less from audiovisual input and show poorer lip-reading skills than CI-CHD users. However, we expected a delay in cortical responses in the CI-SSD group, similar to the group of CI-CHD users, when compared to NH individuals, based on previous results from studies with purely auditory stimuli comparing the CI and the NH ear (Finke, Sandmann, et al., 2016; Bönitz et al. 2018; Weglage et al., 2022)."

In addition to the changes made in the introduction and the discussion, as mentioned before

(introduction: page 4, line 131-136; discussion: page 27, line 960-969), we added specific hypotheses for each analysis step within the methods section to make it more clear to the reader, why we performed these analyses. We did the same analyses as in our previous study to ensure that a direct transferability of results can be made.

Page 10, line 316-320: *“As the hit rates were very high in our previous study (Layer et al., 2022), we did not expect CI-SSD users to deviate from this pattern. Concerning the RTs, we expected similar results for CI-SSD users as for CI-CHD users and NH listeners, with shorter RTs for AV conditions compared to unisensory (A, V) conditions.”*

Page 10, line 349-352: *“Here, we expected a similar redundant signals effect for CI-SSD users, as CI-CHD users and NH listeners both showed a violation of the race model inequality in our previous study (Layer et al., 2022).”*

Page 10-11, line 356-361: *“Concerning the lip-reading ability, we anticipated that CI-SSD users performed worse compared to CI-CHD users due to their intact contralateral ear, which may reduce the need to rely on lip movements in their everyday life. In terms of subjective exertion rating, we expected no difference between experimental groups because our previous study (Layer et al., 2022) found no difference, which was likely due to the easy task.”*

Page 12, line 427-431: *“Based on previous observations with CI-CHD users (Beynon et al., 2005; Finke, Büchner, et al., 2016; Henkin et al., 2014; Sandmann et al., 2009; Layer et al. 2022) and CI-SSD users (Finke, Sandmann, et al., 2016; Bönitz et al. 2018; Weglage et al., 2022), we expected delayed N1 and reduced P2 responses for all CI user groups compared to NH controls.”*

Page 13, line 472-477: *“We anticipated that the analysis of the first onset of maps would confirm a delayed N1 latency for both CI-CHD and CI-SSD users based on previous results. In terms of map presence at N1 latency range, we speculated that there would be a pattern between CI-CHD users and NH listeners for CI-SSD users, as they have both a CI and a NH ear. However, we are not aware of previous studies reporting similar results for CI-SSD users.”*

Page 14, line 514-521: *“Similar to our hypotheses for the fitting data, we speculated that a pattern between the one of CI-CHD users and NH listeners would emerge for the recruitment of the visual cortex, which we observed for CI-CHD users in our previous study (Layer et al., 2022). In addition, in accordance with the fitting data and the GFP, we expected a delayed auditory cortex response for CI-SSD users as well. Finally, based on our previous study, we expected to find indications for multisensory processing, with different activity for AV-V compared to A for CI-SSD users, too.”*

Comment 2:

I wonder whether the authors should acknowledge (discussion) the possibility that the observed effects could emerge with other types of A-V stimuli and not necessarily pertain to language processing.

Response to Comment 2:

Thank you for asking this general and important question. We now discuss this issue in a “limitations” section in the manuscript (page 32, line 1125-1145):

“One might ask the question whether the presented results are transferrable to other audiovisual stimuli or whether these are restricted to language-specific stimuli. We assume that the significant audiovisual benefit observed in our CI users was strongly driven by the linguistic property of the presented stimuli, and we hypothesise that this audiovisual benefit may even be more pronounced for more difficult linguistic stimuli (words or sentences). Nevertheless, when solely focusing on the additional recruitment of the visual cortex, as observed in the present and our recent results (Layer et al., 2022), previous studies have suggested that this effect is not restricted to purely linguistic tasks. This effect has been

shown for syllables, words and environmental sounds (Giraud, Price, Graham, Truy, et al., 2001). Another study (Chen et al., 2016) extended these results to pure tones and reversed words, showing that intelligibility is not necessary for eliciting auditory-induced recruitment of the visual cortex. However, these previous studies do not provide answers concerning processing differences and similarities between CI user groups, which is the novelty of this study. We hypothesise that further and more pronounced differences between CI-CHD users and CI-SSD users will become evident for more difficult linguistic stimuli (words/sentences vs. syllables) and more difficult task conditions (semantic processing vs. discrimination of syllables). Importantly, future studies should use the same experimental settings (i.e. the same paradigm) for different types of stimuli. They should compare cortical response patterns between non-linguistic stimuli (e.g. basic and environmental sounds) and linguistic stimuli (e.g., syllables and words), to see if our findings are transferable to both non-linguistic and more difficult linguistic stimulus conditions within the same patients.”

Comment 3:

Figures. ERPs and source timeseries of the data in the source domain would benefit from having SE included as shaded region.

Response to Comment 3:

Thank you for this great suggestion. We changed Figure 2 and Figure 4 accordingly.

Comment 4:

It would be relevant to have access to the stimuli

Response to Comment 4:

Thank you for raising this point. We agree that we should share our video files, given that we also benefited from the free availability of the words used in the current study's lip-reading task (Stropahl et al. 2015). Therefore, we uploaded the stimuli (video files) as supplementary material and mentioned this in the manuscript (page 8, line 250-251).

Comments from Reviewer 2

Reviewer 2: The authors present a study that is follow up to a previously published paper. The only thing that appears to be really different in this study is the addition of an SSD group (the comparison data is identical to the previously published data). I will leave it to the editor to determine if this in itself is worthy of a separate publication.

The methods are sound.

Comment 1:

The biggest effect is that of the P2. In the auditory condition, there is a large P2 response for the auditory condition. The authors only report the AV-V condition. This is pretty annoying and I would have liked to have seen the all three conditions overlaid. I understand that the authors are comparing additive effects models, but, nonetheless, having see the raw data for visual only would be nicer and give a more complete picture.

Response to comment 1:

Thank you for making such an important and reasonable observation. We agree that showing the ERPs separately for each condition is critical in order for other researchers to validate and compare the waveforms from their experiments. We admit that this information is missing in this paper and have decided to include it in a supplementary material file (see supplementary material). This supplementary material is now mentioned in the manuscript (page 17, line 584-586).

Comment 2:

What is contributing to the P2? What is the dominant generator? (aside from the ROIs listed)
How do these data correlate to speech perception?

Response to comment 2:

Thank you for these important and fundamental questions. Previous studies report that the P2 is related to age, learning, training and memory (Ross & Tremblay, 2009 *Hearing Research*; Tremblay et al., 2014 *Frontiers in System Neuroscience*). It has also been linked to higher-order perceptual and attentional processing (Luck & Hillyard, 1994 *Psychophysiology*) as well as top-down matching processes (Federmeier et al., 2005 *Memory and Cognition*). Furthermore, it has been proposed that the P2 may index implicit, higher-order perceptual processes that occur when a stimulus is compared to mental representations that were either stored in memory or constructed from a linguistic context (Evans & Federmeier, 2007 *Neuropsychologia*). In addition, it has been linked to higher-level perceptual processes involved in target identification (Crowley and Colrain, 2004 *Clinical Neurophysiology*). Finally, according to a recent study, the P2 is influenced by spatially selective brain activity, which is influenced crossmodally by visual information (Shrem et al., 2017 *Psychophysiology*).

Regarding the sources of the P2, previous studies using MEG or fMRI have reported that the auditory P2 is generated in the anterior part of the auditory cortex, in particular the lateral part of the Heschl's gyrus (Bosnyak et al., 2004 *Cerebral Cortex*; Ross & Tremblay, 2009 *Hearing Research*; Tremblay et al., 2014 *Frontiers in System Neuroscience*, Hari et al., 1987 *Audiology*; Pantev et al., 1996 *Ear and Hearing*). In addition, the planum temporale has been reported as source for the P2 ERP (Crowley and Colrain, 2004 *Clinical Neurophysiology* (for review); Godey et al., 2001 *Clinical Neurophysiology*, Hari et al., 1987 *Audiology*). Based on these previous findings, we used an auditory ROI for our ERP source analyses, including the aforementioned cortical regions. Interestingly, other regions, for instance the mesencephalic reticular activating system, may contribute to the P2 ERP as well (Crowley and Colrain, 2004 *Clinical Neurophysiology* (for review); Knight et al., 1980 *Electroencephalography and Clinical Neurophysiology*; Woods et al., 1993 *Cognitive Brain Research*), but there is no universal agreement on it.

One may argue that our selected auditory ROI was not appropriate enough for the analyses of the P2 responses. However, the auditory ROI selected in our study comprised several cortical regions that have been proposed as source of the P2 ERP (e.g. Hari et al., 1987 *Audiology*; Ross & Tremblay, 2009 *Hearing Research*; Bosnyak et al., 2004 *Cerebral Cortex*). In ideal conditions, EEG source analysis may have a spatial resolution of approximately 2 cm (Klamer et al., 2014 *Brain Topography*), which is however ensured only when using individual head models for each participant, which is not the case in the

current study. Therefore, we believe it is better to choose larger ROIs for analyses, which also considers the variance across individuals regarding the location of the maximal cortical activation. To clarify that our chosen auditory ROI was based on reported sources in the literature, we added an additional sentence in the manuscript:

Page 14, line 503-506: “In specific, the chosen parts of the auditory ROI have been reported as both N1 (Näätänen & Picton, 1987; Godey et al., 2001; Woods et al., 1993; Bosnyak et al., 2004) and P2 (Crowley and Colrain, 2004 (for review); Hari et al., 1987; Bosnyak et al., 2004; Ross & Tremblay, 2009) generators.”

As we did not have any specific hypotheses concerning possible relationships between the P2 and speech perception, we did not calculate any correlations for this. We reduced the risk for alpha error (multiple comparison problem) and reduced the number of correlations as best as possible by focusing on correlations reported in previous studies (Layer et al., 2022 *NeuroImage: Clinical*; Stropahl et al., 2015 *NeuroImage*; Stropahl & Debener, 2017 *NeuroImage*; Giraud, Price, Graham, Truy, et al., 2001 *Neuron*). However, based on the question of the Reviewer, we calculated explorative correlations between the P2 GFP amplitude, the P2 amplitude in the visual cortex and the P2 amplitude in the auditory cortex with the score of the speech test (Freiburg monosyllabic test), separately for CI-SSD and CI-CHD users. The results revealed no significant correlations between the P2 response and the speech recognition ability. The exact correlation values can be found in the table below.

Amplitude	Group	r-value	p-value
P2 GFP	CI-CHD	0.359	0.343
P2 GFP	CI-SSD	0.0895	0.585
P2 visual ROI	CI-CHD	-0.0973	0.803
P2 visual ROI	CI-SSD	-0.129	0.723
P2 auditory ROI	CI-CHD	-0.0824	0.833
P2 auditory ROI	CI-SSD	-0.404	0.247

We refrained from including this supplementary analysis into the manuscript, as our results did not reveal any significant correlation between the P2 response and the speech perception.

Comment 3:

I would like to see some more discussion of the differences between SSD and CHD. This is really the whole point of the paper!

Response to comment 3:

Thank you for this important remark. We fully agree with the Reviewer’s concern and added some further sentences in the discussion on the differences between CI-SSD and CI-CHD users, both in the introduction and the discussion:

- 1) Introduction: page 4, line 131-136: *“This is noteworthy because literature comparing CI-SSD to bimodal or bilateral CI users is scarce. However, the few existing studies reported differences in speech-in-noise performance (Williges et al., 2019) and in situations with multiple concurrent speakers (Bernstein et al., 2016) between CI-SSD users and bimodal or bilateral CI users,*

respectively. But, given this first evidence for purely auditory situations, we hypothesised that further differences would emerge for audiovisual stimulation, which has yet to be reported.”

- 3) Discussion: page 28, line 965-974: *“Previous research comparing different groups of CI users is limited. Nevertheless, first evidence of differences in speech-in-noise performance between CI-SSD users and bimodal CI users (CI on one ear and hearing aid on the contralateral ear) was reported (Williges et al., 2019). On the other hand, differences between CI-SSD users and bilateral CI users (both ears fitted with CIs) were observed in situations with multiple concurrent speakers (Bernstein et al., 2016). As a result, we expected group differences to emerge not only for auditory stimulation but also for audiovisual stimulation. However, as far as we are aware, this has not been investigated yet. Our results therefore indeed confirm first indications of different processing strategies among different CI user groups.”*

Besides, we would like to emphasise that this paper discussed not only the differences, but also the similarities in auditory, visual and audiovisual speech processing between the two CI user groups. We believe, they are as important and as insightful as the differences, particularly the novel and unexpected finding on the lip-reading abilities in the CI-SSD user group, which were comparable to those of the bilateral CI users. This study is a first attempt to characterise differences and similarities among CI user groups in audiovisual speech processing, with the goal of encouraging other researchers to design follow-up studies in this area. However, we agree that the original title of our manuscript may be a little misleading, giving the impression that the differences are not discussed thoroughly and that this is the only topic covered in this paper. To avoid misunderstandings, we changed the title to "Electrophysiological differences *and similarities* in audiovisual speech processing in CI users with unilateral and bilateral hearing loss." In addition, we added a short sentence within the conclusion (page 32, line 1160): *“This auditory-induced activation in the visual cortex is an important and insightful similarity between the two CI user groups.”*

Accept Letter

Dear Mrs. Layer,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I am pleased to inform you that your manuscript has been accepted for publication.

My comments, and any reviewer comments, are below.

Your accepted manuscript will now be transferred to our production department. We will create a proof which you will be asked to check, and you will also be asked to complete a number of online forms required for publication. If we need additional information from you during the production process, we will contact you directly.

We appreciate you submitting your manuscript to Current Research in Neurobiology and hope you will consider us again for future submissions.

Kind regards,

Kerry Walker, DPhil
Associate Editor
Current Research in Neurobiology

Editor and Reviewer comments:

The authors have taken each of the reviewer's original concerns into consideration and have addressed them in their revised manuscript. I apologise on behalf of our journal for the delay in this final decision, as we were unable to receive the second round of reviews in a timely manner. However, I am satisfied based on my own assessment of the manuscript and the favourable assessment of Reviewer 1, that this manuscript is now ready for acceptance in Current Research in Neurobiology. Congratulations!

Reviewer 2: All of my issues have been addressed

----- *End of Review Comments* -----