

# Dorsolateral prefrontal cortex supports speech perception in listeners with cochlear implants

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## Abstract

21 Cochlear implants are neuroprosthetic devices that can restore hearing in individuals with severe  
 22 to profound hearing loss by electrically stimulating the auditory nerve. Because of physical  
 23 limitations on the precision of this stimulation, the acoustic information delivered by a cochlear  
 24 implant does not convey the same level of spectral detail as that conveyed by normal hearing. As  
 25 a result, speech understanding in listeners with cochlear implants is typically poorer and more  
 26 effortful than in listeners with normal hearing. The brain networks supporting speech  
 27 understanding in listeners with cochlear implants are not well understood, partly due to difficulties  
 28 obtaining functional neuroimaging data in this population. In the current study, we assessed the  
 29 brain regions supporting spoken word understanding in adult listeners with right unilateral  
 30 cochlear implants (n=20) and matched controls (n=18) using high-density diffuse optical  
 31 tomography (HD-DOT), a quiet and non-invasive imaging modality with spatial resolution  
 32 comparable to that of functional MRI. We found that while listening to spoken words in quiet,  
 33 listeners with cochlear implants showed greater activity in the left dorsolateral prefrontal cortex,  
 34 overlapping with functionally-defined domain-general processing seen in a spatial working  
 35 memory task. These results suggest that listeners with cochlear implants require greater cognitive  
 36 processing during speech understanding than listeners with normal hearing, supported by  
 37 compensatory recruitment in the left dorsolateral prefrontal cortex.

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## Introduction

41 Cochlear implants (CIs) are neuroprosthetic devices that can restore hearing in individuals with  
42 severe to profound hearing loss by electrically stimulating the auditory nerve. Because of physical  
43 limitations on the precision of this stimulation—including, for example, the spatial spread of  
44 electrical current (Garcia, Goehring et al. 2021)—the auditory stimulation delivered by a CI does  
45 not convey the same level of spectral detail as normal hearing. As a result, speech understanding  
46 in listeners with CIs is poorer than in listeners with normal hearing (Firszt, Holden et al. 2004).  
47 Notably, even in quiet, listeners with CIs report increased effort during listening (Dwyer, Firszt et  
48 al. 2014). In spite of these challenges, many listeners with CIs attain significant levels of auditory  
49 speech understanding. This remarkable success raises the question of how listeners with CIs  
50 make sense of a degraded acoustic signal.

51 One area of key importance is understanding the degree to which listeners with CIs rely  
52 on nonlinguistic cognitive mechanisms to compensate for a degraded acoustic signal. In listeners  
53 with normal hearing, cognitive demands are increased when speech is acoustically challenging  
54 (Peelle 2018). For example, even when speech is completely intelligible, acoustically-degraded  
55 speech is more difficult to remember than acoustically clear speech (Rabbitt 1968, Cousins, Dar  
56 et al. 2014, Ward, Rogers et al. 2016, Koeritzer, Rogers et al. 2018). These findings suggest that  
57 to understand acoustically challenging speech, listeners need to engage domain-general  
58 cognitive resources. In a limited-capacity cognitive system (Wingfield 2016), such recruitment  
59 necessarily reduces the resources available for other tasks, such as memory encoding.

60 Cognitive demands during speech understanding are supported by several brain networks  
61 that supplement classic frontotemporal language networks. The cingulo-opercular network, for  
62 example, is engaged during particularly challenging speech (Eckert, Menon et al. 2009, Vaden,  
63 Teubner-Rhodes et al. 2017) and supports successful comprehension during difficult listening  
64 (Vaden, Kuchinsky et al. 2013). The activity in dorsolateral prefrontal cortex (DLPFC)  
65 complements the cingulo-opercular network and varies parametrically with speech intelligibility  
66 (Davis and Johnsrude 2003). Activity in DLPFC is associated with cognitive demands in a wide  
67 range of tasks (Duncan 2010), consistent with domain-general cognitive control (Braver 2012).  
68 However, the functional anatomy of DLPFC is also complex (Noyce, Cestero et al. 2017), and  
69 dissociating nearby language and domain-general processing regions is challenging (Fedorenko,  
70 Duncan et al. 2012).

71 Then, a central question concerns the degree to which listeners with CIs rely on cognitive  
72 processing outside core speech processing regions, such as DLPFC. Obtaining precise spatially-  
73 localized images of regional brain activity has been difficult in listeners with CIs, given that  
74 functional MRI is not possible (or subject to artifact) due to the CI hardware. Thus, optical brain  
75 imaging (Peelle 2017) has become a method of choice for studying functional activity in CI  
76 listeners (Lawler, Wiggins et al. 2015, Olds, Pollonini et al. 2016, Anderson, Wiggins et al. 2017,  
77 Lawrence, Wiggins et al. 2018, Zhou, Seghouane et al. 2018). In the current study, we use high-  
78 density diffuse optical tomography (HD-DOT) (Eggebrecht, Ferradal et al. 2014), previously  
79 validated in speech studies in listeners with normal hearing (Hassanpour, Eggebrecht et al. 2015,  
80 Hassanpour, Eggebrecht et al. 2017, Schroeder, Sherafati et al. 2020). HD-DOT provides high  
81 spatial resolution and homogenous sensitivity over the field of view that captures known speech-  
82 related brain regions (White and Culver 2010). We examine the brain regions supporting single  
83 word processing in listeners with a right unilateral CI relative to that in a group of matched controls.  
84 We hypothesized that listeners with CIs would exhibit greater recruitment in regions of DLPFC  
85 compared to normal hearing controls.

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## Methods

### Data and code availability

Summary data and analysis scripts are available in [https://osf.io/nkb5v/?view\\_only=2c8ef3af126542a49be055d50ac935d4](https://osf.io/nkb5v/?view_only=2c8ef3af126542a49be055d50ac935d4).

### Subjects

We recruited 21 adult CI patients and 19 age- and sex-matched controls (demographic information in **Table 1**). We excluded one CI user due to poor signal quality (evaluated as mean band limited SNR of all source-detectors) and one control due to excessive motion (see **Fig. S6**, and **supplementary materials** for details). All patients had a unilateral right CI and controls had normal bilateral hearing. All subjects were native speakers of English with no self-reported history of neurological or psychiatric disorders. All aspects of these studies were approved by the Human Research Protection Office of the Washington University School of Medicine. Subjects were recruited from the Washington University campus and the surrounding community (IRB 201101896, IRB 201709126). All subjects gave informed consent and were compensated for their participation in accordance with institutional and national guidelines.

**Table 1:** Demographic information.

Population	Control	CI users
Number of subjects (# of females)	18 (10)	20 (11)
Mean age at test in years (std)	56.05 (12.26)	56.80 (14.09)
Mean years of CI use (std)	NA	8.10 (6.51)
Mean speech perception score (AzBioSentences) (std), max = 1	0.99 (0.01)	0.88 (0.09)
Mean right ear 4fPTA* (std)	16.02 (6.74)	21.85 (5.30) with CI on
Mean left ear 4fPTA* (std)	16.61 (7.67)	91.25 (26.77) unaided
Mean left ear 4fPTA* at test <sup>1</sup> (std)	NA	73.28 (37.72)
Mean duration of deafness right ear	NA	12.58 (11.74)

\*4fPTA, pure tone average at 4 frequencies, 500, 1000, 2000, 4000 Hz.

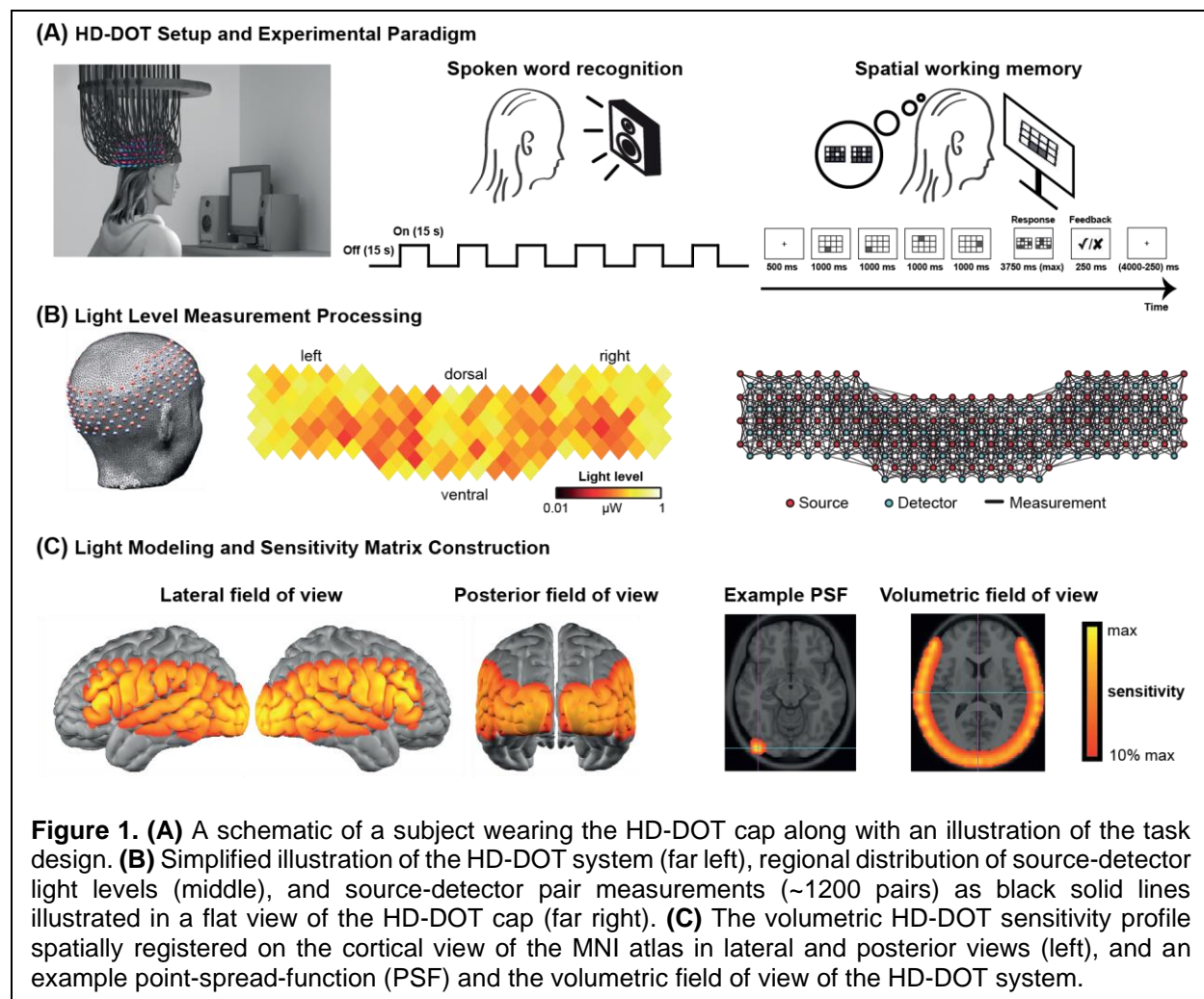
If no response at a given frequency, a value of 120 dB HL was assigned.

<sup>1</sup> With hearing aid, if the subject used amplification. Eight out of twenty CI users had hearing aids.

### HD-DOT system

Data were collected using a continuous-wave HD-DOT system comprised of 96 sources (LEDs, at both 750 and 850 nm) and 92 detectors (coupled to avalanche photodiodes, APDs, Hamamatsu C5460-01) to enable oxy and deoxyhemoglobin spectroscopy (**Fig. 1**) (Eggebrecht, Ferradal et al. 2014). The design of this HD-DOT system provides more than 1200 usable source-detector measurements at a 10 Hz full-field frame rate. This system has been validated for successfully mapping cortical responses to hierarchical language paradigms and naturalistic stimuli with comparable sensitivity and specificity to fMRI (Eggebrecht, Ferradal et al. 2014, Hassanpour, Eggebrecht et al. 2015, Fishell, Burns-Yocum et al. 2019).

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**Figure 1. (A)** A schematic of a subject wearing the HD-DOT cap along with an illustration of the task design. **(B)** Simplified illustration of the HD-DOT system (far left), regional distribution of source-detector light levels (middle), and source-detector pair measurements (~1200 pairs) as black solid lines illustrated in a flat view of the HD-DOT cap (far right). **(C)** The volumetric HD-DOT sensitivity profile spatially registered on the cortical view of the MNI atlas in lateral and posterior views (left), and an example point-spread-function (PSF) and the volumetric field of view of the HD-DOT system.

## Experimental design

Subjects were seated on a comfortable chair in an acoustically isolated room facing an LCD screen located 76 cm from them, approximately at their eye level. The auditory stimuli were presented through two speakers located approximately 150 cm from the subjects' ears. Subjects were instructed to fixate on a white crosshair against a gray background while listening to the auditory stimuli, holding a keyboard on their lap for the stimuli that required their response (**Fig. 1A**, left panel). The HD-DOT cap was fitted to the subject's head to maximize optode-scalp coupling, assessed via real-time coupling coefficient readouts using an in-house software. The stimuli were presented using Psychophysics Toolbox 3 package (Brainard 1997) (RRID:SCR\_002881) in MATLAB 2010b.

The spoken word recognition paradigm consisted of six blocks of spoken words per run. Each block contained 15 seconds of spoken words (one word per second), followed by 15 seconds of silence. Two runs were performed in each study session with a total of 180 words in about 6 minutes (**Fig. 1A**, middle panel).

Based on indications of DLPFC activity in our preliminary results, we adopted the spatial working memory task introduced in previous studies (Fedorenko, Behr et al. 2011, Fedorenko, Duncan et al. 2013) in the remaining subjects to aid in functionally localizing domain-general



regions of the prefrontal cortex. In this spatial working memory task, subjects were asked to remember four locations (easy condition) or eight locations (hard condition) in a 3x4 grid. Following each trial, subjects had to choose the pattern they saw among 2-choice grids, one with correct and one with incorrect locations. This task requires keeping sequences of elements in memory for a brief period and has been shown to activate DLPFC (**Fig. 1A**, right panel). Each run for the spatial working memory task was about 8 minutes, with a total of 48 trials in the run.

## Data processing

HD-DOT data were pre-processed using the NeuroDOT toolbox (A. T. Eggebrecht 2019). Source-detector (SD) pair light level measurements were converted to log-ratio by calculating the temporal mean of a given SD-pair measurement as the baseline for that measurement. Noisy measurements were empirically defined as those that have greater than 7.5% temporal standard deviation in the least noisy (lowest mean motion) 60 seconds of each run (Eggebrecht, Ferradal et al. 2014, Sherafati, Snyder et al. 2020). Then, channels with greater than 33% noisy first or second nearest neighbor measurements (nn1 and nn2) were excluded (**Fig. S4**). The data were next high pass filtered at 0.02 Hz. The global superficial signal was estimated as the average of the nn1 measurements (13 mm SD-pair separation) and regressed from the data (Gregg, White et al. 2010). The optical density time-courses were then low pass filtered to 0.5 Hz to the physiological brain signal band and temporally downsampled from 10 Hz to 1 Hz. A wavelength-dependent forward model of light propagation was computed using the ICBM152 anatomical atlas using the non-uniform tissue structures: scalp, skull, CSF, gray matter, and white matter (Ferradal, Eggebrecht et al. 2014) (**Fig. 1C**). Relative changes in the concentrations of oxygenated, deoxygenated, and total hemoglobin ( $\Delta\text{HbO}$ ,  $\text{HbR}$ ,  $\Delta\text{HbT}$ ) were obtained from the absorption coefficient changes by the spectral decomposition of the extinction coefficients of oxygenated and deoxygenated hemoglobin at the two wavelengths (750 nm and 850 nm). After inverting the sensitivity matrix, relative changes in absorption at the two wavelengths were reconstructed using Tikhonov regularization and spatially variant regularization (Eggebrecht, Ferradal et al. 2014). After post-processing, we resampled all data to the  $3 \times 3 \times 3 \text{ mm}^3$  MNI atlas using a linear affine transformation for group analysis. In addition to the standard HD-DOT pre-processing steps used in the NeuroDOT toolbox, we used a comprehensive data quality assessment pipeline (**Supplementary materials**) to exclude the data runs with low heartbeat SNR or high motion levels.

After pre-processing, the response for the speech task was estimated using a standard general linear model (GLM) framework. The design matrix was constructed using onsets and durations of the stimulus presentation convolved with a canonical hemodynamic response function (HRF). This HRF was created using a two-gamma function (2 s delay time, 7 s time to peak, and 17 s undershoot) fitted to the HD-DOT data described in a previous study (Hassanpour, Eggebrecht et al. 2015). We included both runs for each subject in one design matrix using custom MATLAB scripts (**Fig. S3A**).

For modeling the spatial working memory task, we used a standard GLM with two columns representing easy and hard conditions. The duration of each easy or hard trial was modeled as the total time of stimulus presentation and evaluation. Events were convolved with the same canonical HRF described in the spoken word perception task to model hemodynamic responses (Hassanpour, White et al. 2014). Due to the novelty of this task for CI users and an age-matched control group, we have used the easy + hard response maps as a reference for defining the DLPFC ROI (as opposed to the hard > easy previously used for younger populations).

After estimating the response ( $\beta$  map) for each subject for each task, we performed a second-level analysis in SPM12 (RRID:SCR\_007037). Extracted time traces for each subject were then calculated using a finite impulse response model.

We only present the  $\Delta\text{HbO}$  results in the main figures as we have found that the  $\Delta\text{HbO}$  signal exhibits a higher contrast-to-noise ratio compared to  $\Delta\text{HbR}$  or  $\Delta\text{HbT}$  (Eggebrecht, Ferradal et al. 2014, Hassanpour, White et al. 2014).

## Region of interest analysis

To perform a more focused comparison between controls and CI users, we objectively defined three regions of interest (ROIs), independent from our spoken word recognition dataset for statistical analysis.

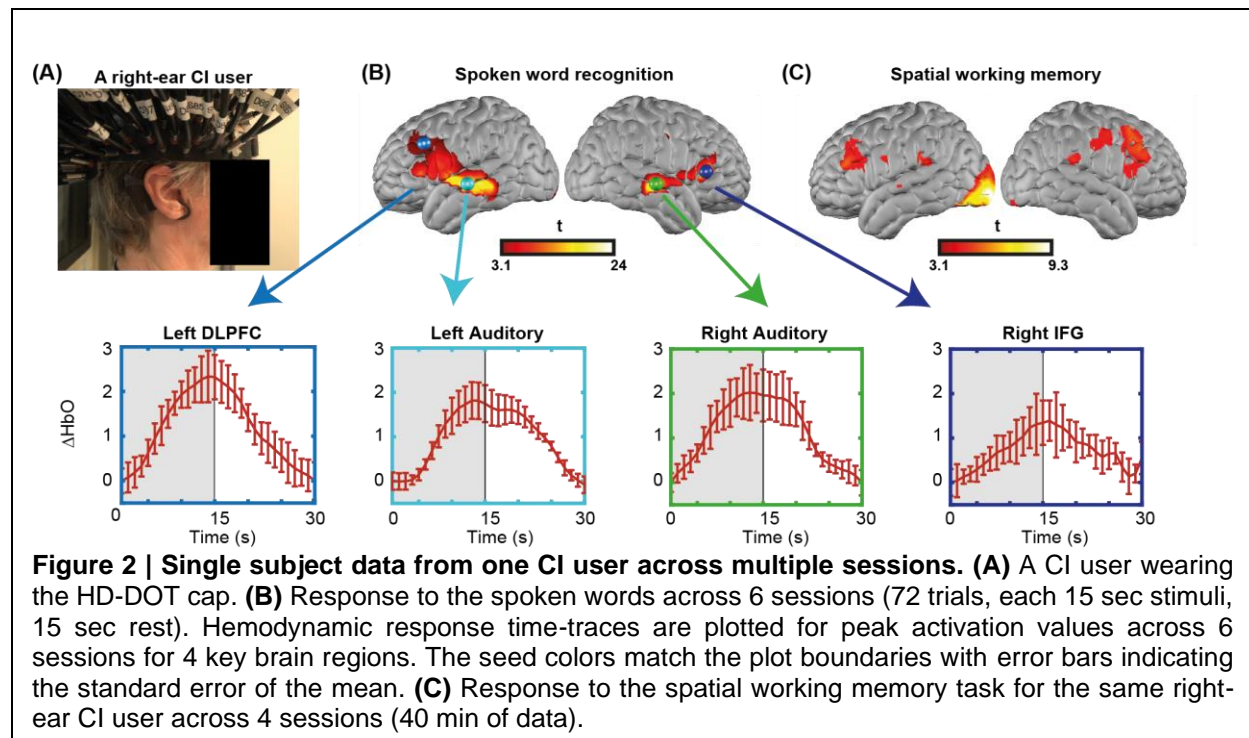
We defined the left DLPFC ROI based on the response of the spatial working memory task in a group of subjects using the cluster of activation around the DLPFC region after  $p < 0.05$  (uncorrected) voxelwise thresholding.

To define the left and right auditory ROIs, we used a previously published fMRI resting state dataset (Sherafati, Snyder et al. 2020) that was masked by the field of view of our HD-DOT system. We defined the left and right auditory ROIs by selecting a 5 mm radius seed in the contralateral hemisphere ([70.5, -24, 3], [-67.5, -27, 3]) and finding the Pearson correlation between the time-series of the seed region with all other voxels in the field of view. Correlation maps in individuals were Fisher's z-transformed and averaged across subjects. More details are provided in the results section.

## Results

### Multi-session single subject results

Due to the expected variability across CI users and difficulties in defining single subject ROIs, we performed a small multi-session study from one of our CI subjects for 6 sessions (**Fig. 2**). We collected 2 runs of spoken word perception per session (for 6 sessions) and 1 run of spatial working memory task per session (for 4 sessions). This multi-session analysis enabled localizing



the left and right DLPFC based on the non-verbal spatial working memory task for this subject (Fig. 2C). It also revealed the engagement of regions beyond the auditory cortex, including the DLPFC during the word perception task (Fig. 2B). Time-traces of oxyhemoglobin concentration change show a clear event-related response for four selected regions in the word perception results (Fig. 2).

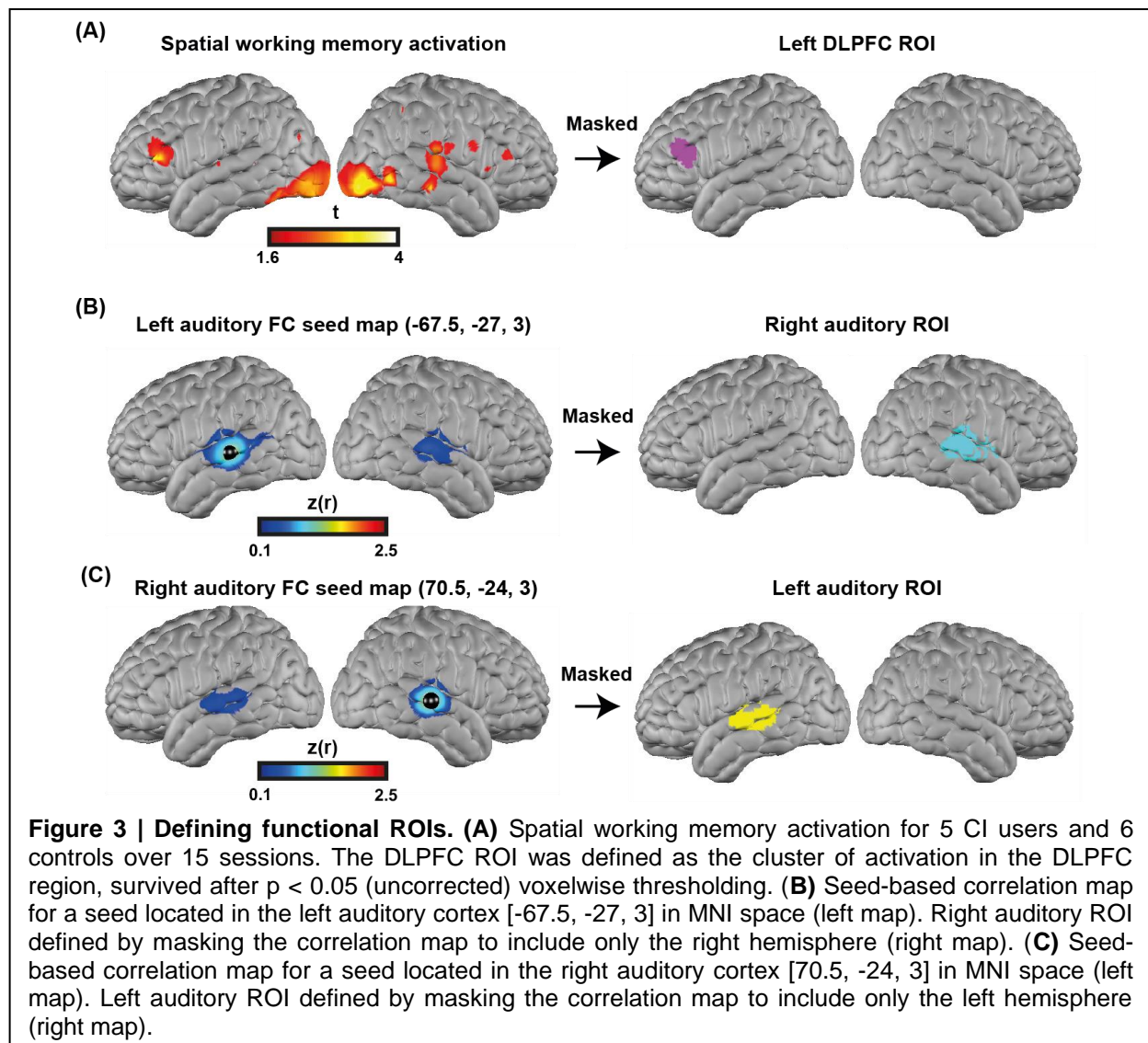
### Functionally defined ROIs

To accurately localize the elevated prefrontal cortex activation in the CI group, we collected HD-DOT data from 11 subjects (6 controls and 5 CI users in 15 sessions) using a spatial working memory task. This task robustly activates DLPFC due to its working memory demands (and visual cortex because of its visual aspect). We chose this task to better localize the DLPFC ROI for performing an ROI-based statistical analysis between controls and CI users. Our results show strong bilateral visual and DLPFC activations in response to this task (Fig. 3A left). We then defined the left DLPFC ROI as the cluster of activation in the left DLPFC region, as described in the methods section (Fig. 3A right).

We defined the left and right auditory ROIs by selecting a seed in the opposite hemisphere (as described in the methods) and finding the Pearson correlation between the time-series of the seed region with all other voxels in the field of view. Correlation maps in individuals were Fisher's z-transformed and averaged across subjects (Fig. 3B-C left). Right/left auditory ROIs were defined by masking the correlation map to include only the right/left hemisphere (Fig. 3B-C right).



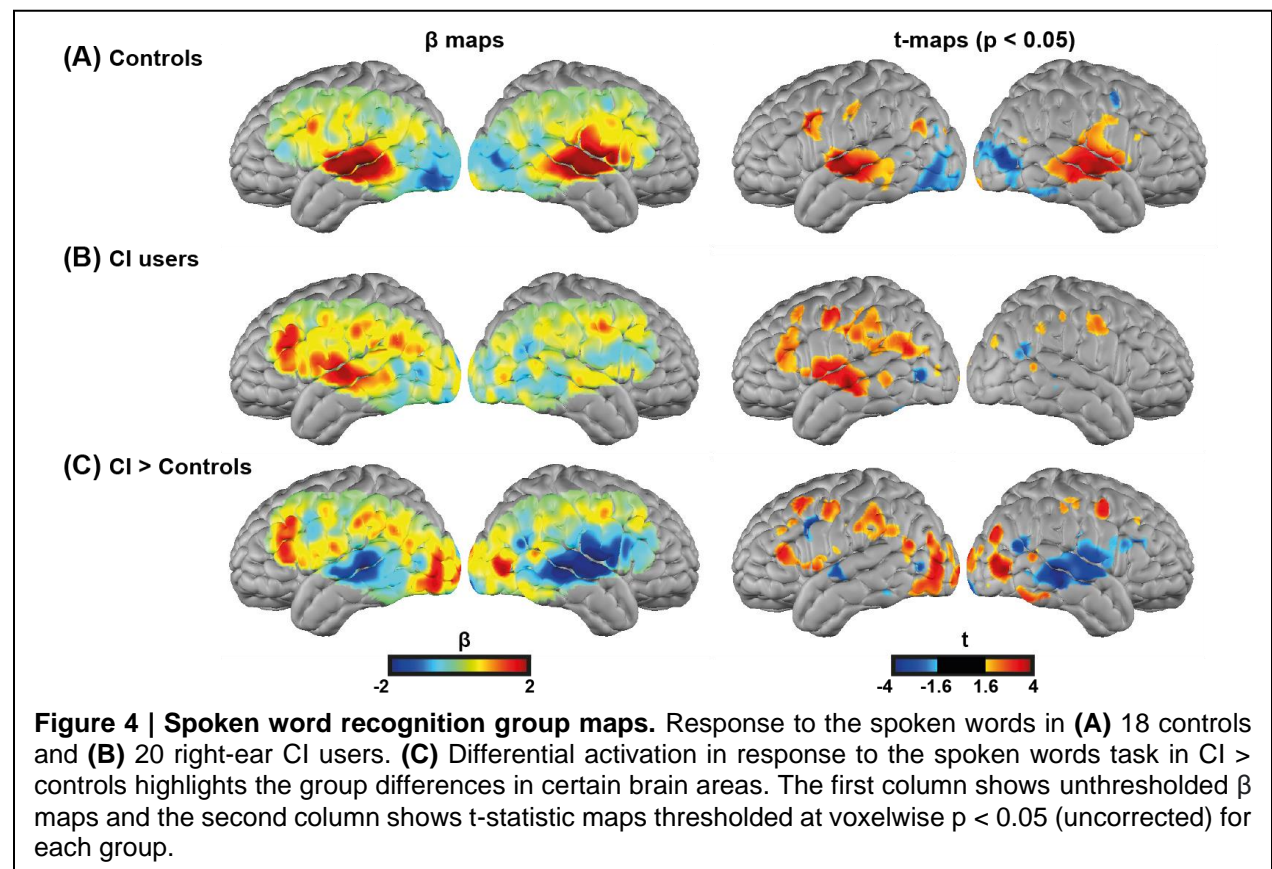
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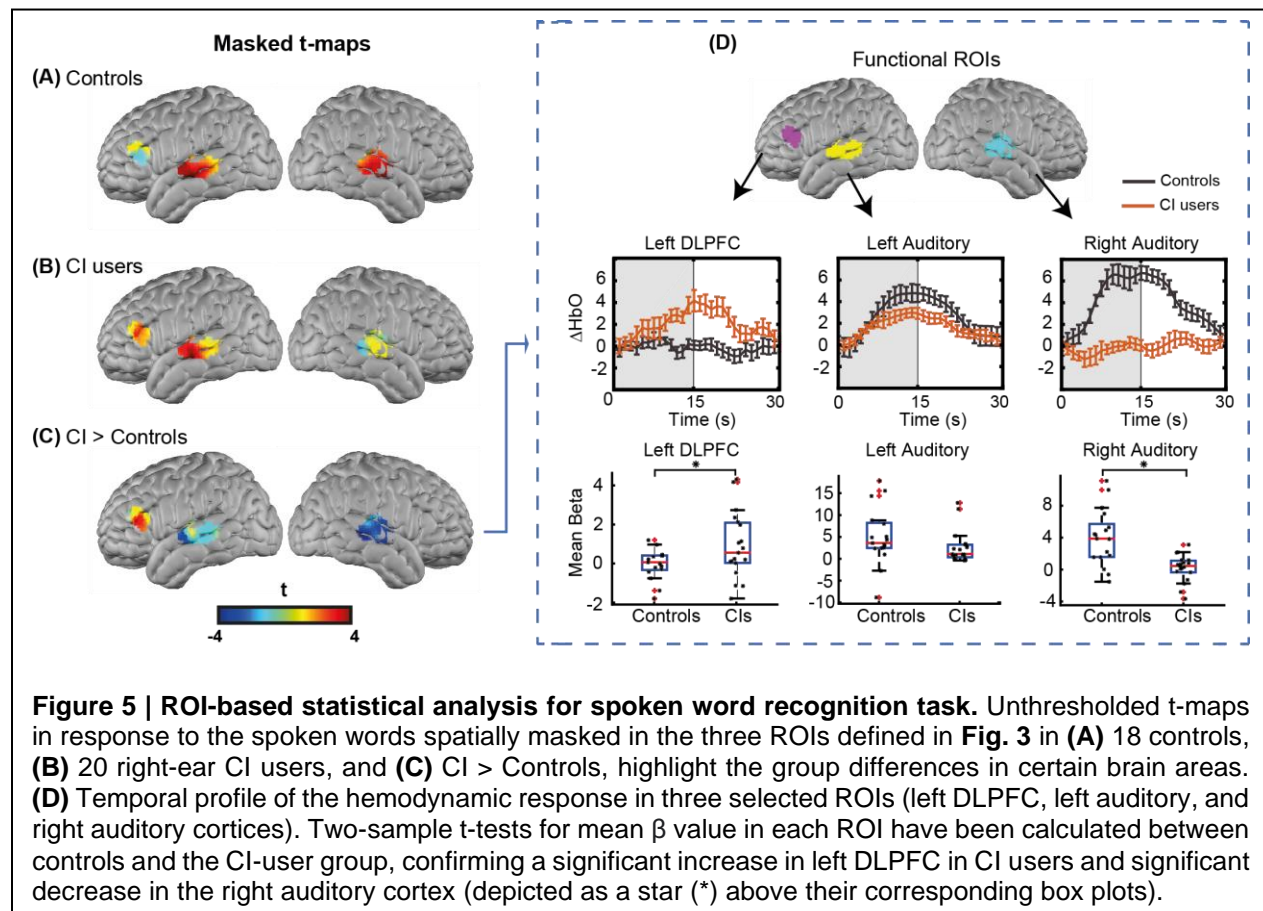
## 234 Mapping the brain response to spoken words

235 We first investigated the degree of auditory activation in both control and CI groups by assessing  
 236 the activity in a block-design single word presentation task. We found strong bilateral superior  
 237 temporal gyrus (STG) activations in controls similar to our previous studies using the same  
 238 paradigm (Eggebrecht, Ferradal et al. 2014, Hassanpour, Eggebrecht et al. 2015), as well as a  
 239 strong left STG and a smaller right STG activation for the CI users (**Fig. 4A-B**). In addition, we  
 240 observed strong left-lateralized activations in regions beyond the auditory cortex, including parts  
 241 of the prefrontal cortex in the CI user group (**Fig. 4B**). The temporal profile of the hemodynamic  
 242 response in three selected ROIs also reflects the increased activity in the left DLPFC region in  
 243 the CI users relative to controls, and a decrease in both left and right auditory cortical regions.  
 244 Two sample t-statistics for the mean  $\beta$  values in each ROI support a statistically significant  
 245 difference between the control and CI groups in left DLPFC and right auditory cortex (**Fig. 5D**).

**Figure S7** provides the  $\beta$  maps of oxyhemoglobin (HbO), deoxyhemoglobin (HbR), and total hemoglobin (HbT) for controls (panel A), CI users (panel B), and CI greater than controls (panel C).



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**Figure 5 | ROI-based statistical analysis for spoken word recognition task.** Unthresholded t-maps in response to the spoken words spatially masked in the three ROIs defined in Fig. 3 in (A) 18 controls, (B) 20 right-ear CI users, and (C) CI > Controls, highlight the group differences in certain brain areas. (D) Temporal profile of the hemodynamic response in three selected ROIs (left DLPFC, left auditory, and right auditory cortices). Two-sample t-tests for mean  $\beta$  value in each ROI have been calculated between controls and the CI-user group, confirming a significant increase in left DLPFC in CI users and significant decrease in the right auditory cortex (depicted as a star (\*) above their corresponding box plots).

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## Behavioral measures

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An important consideration in studying CI users is the variability in their speech perception abilities, hearing thresholds, and the relationship with brain activity. Figure 6 shows exploratory analyses between the magnitude of the activation in the left DLPFC ROI for the CI user cohort with respect to the speech perception score, left ear hearing threshold un-aided, left ear hearing threshold at test (aided if the subject used a hearing aid), and right ear hearing threshold (CI-aided).

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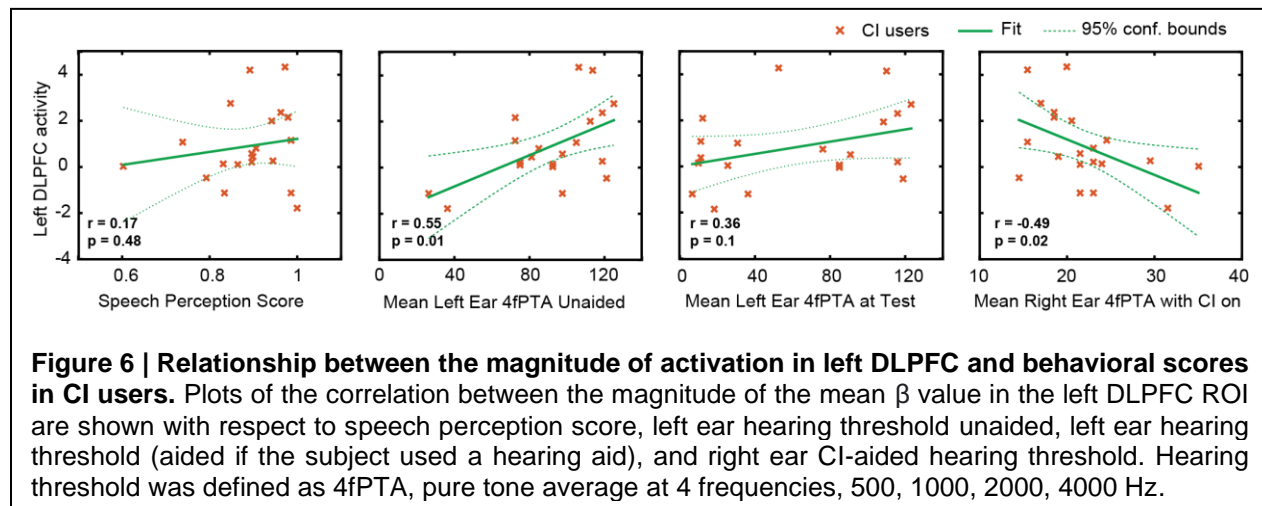
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Using  $p < 0.05$  (uncorrected) as a statistical significance threshold, left DLPFC activation positively correlated with left ear unaided thresholds ( $p = 0.01$ ) and negatively correlated with right ear CI-aided thresholds ( $p = 0.02$ ). Left DLPFC activation did not correlate with speech perception score ( $p = 0.4$ ) and aided hearing threshold for the left ear ( $p = 0.1$ ).

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## Discussion

266 Using high-density optical brain imaging, we examined the brain networks supporting spoken  
 267 word recognition in listeners with CIs relative to a matched group of controls with bilateral normal  
 268 hearing. We found that relative to controls, when listening to words, listeners with CIs showed  
 269 reduced activity in the right auditory cortex and—critically—increased activity in left DLPFC. We  
 270 review these two findings in turn below.

### 271 Reduced auditory cortical activity in CI users

272 We found reduced activity in the right auditory cortex in CI users relative to controls, which we  
 273 attribute to differences in auditory stimulation. We limited our sample to CI listeners with unilateral  
 274 right-sided implants but did not restrict left ear hearing. Most of our subjects with CIs had poor  
 275 hearing in their left ears, which would result in reduced auditory information being passed to the  
 276 contralateral (right) auditory cortex. This was as opposed to controls who had bilateral hearing.  
 277 Prior fNIRS studies have also shown that activity in the superior temporal cortex corresponds with  
 278 stimulation and comprehension (Olds, Pollonini et al. 2016, Zhou, Seghouane et al. 2018).

279 What is potentially more interesting is a lower level of activity in the left auditory cortex of  
 280 the CI users compared to controls, even though all CI listeners were receiving adequate  
 281 stimulation of their right auditory nerve with a right CI. There are several possible explanations for  
 282 this finding. First, activity in superior temporal cortex does not reflect only “basic” auditory  
 283 stimulation, but processing related to speech sounds, word meaning, and other levels of linguistic  
 284 analysis. Thus, although subjects with CIs were certainly receiving stimulation and speech  
 285 intelligibility scores were generally good, some variability was still present (mean speech  
 286 perception score = 0.88, SD = 0.09). The overall level of speech processing was significantly ( $p$  =  
 287 0.00005) lower for CI users than controls (mean speech perception score = 0.99, SD = 0.01),  
 288 resulting in decreased activity (indeed, because the depth of HD-DOT includes only about 1 cm  
 289 of the brain, much of primary auditory cortex is not present in our field of view, and the observed  
 290 group differences were localized in non-primary regions of STG and MTG).

291 Perhaps the most provocative explanation is that a reduction in top-down modulatory  
 292 processes (Davis and Johnsrude 2007) plays out as reduced activity in the temporal cortex. That  
 293 is, given that effortful listening depends on attention (Wild, Yusuf et al. 2012), it might be that



processes related to top-down prediction (Sohoglu, Peelle et al. 2012, Sohoglu, Peelle et al. 2014, Cope, Sohoglu et al. 2017) are muted when too much cognitive control is required for perceptual analysis. Reconciling this interpretation with predictive coding accounts of speech perception (Blank and Davis 2016, Sohoglu and Davis 2020) will require additional work.

### **Increased dorsolateral prefrontal cortex activity in CI users**

When listening to spoken words in quiet, listeners with normal hearing typically engage the left and right superior temporal cortex, including primary and secondary auditory regions (Price, Wise et al. 1992, Binder, Frost et al. 2000, Wiggins, Anderson et al. 2016, Rogers, Jones et al. 2020). Our current results for controls show this same pattern. However, when listeners with CIs performed the same task, we found that they engaged left DLPFC significantly more than the controls.

Although we only tested a single level of speech difficulty (that is, speech in quiet), prior studies have parametrically varied speech intelligibility and found intelligibility-dependent responses in the prefrontal cortex. Use of several types of signal degradation (Davis and Johnsrude 2003), revealed a classic “inverted-U” shape response in the prefrontal cortex as a function of speech intelligibility, with activity increasing until the speech became very challenging and then tapering off. A similar pattern was reported in fNIRS (Lawrence, Wiggins et al. 2018).

A pervasive challenge for understanding the role of DLPFC in speech understanding is the close anatomical relationship of core language processing regions and domain-general regions of prefrontal cortex (Fedorenko et al. 2012). We attempted to add some degree of functional specificity to our interpretation by including a spatial working memory task presumed to strongly engage domain-general regions with minimal reliance on language processing (Duncan 2010, Alexandra, Jade et al. 2015). Ideally, we would have used functional ROIs individually created for each subject, however, we were not convinced that our data were sufficiently reliable at the single-subject level. Furthermore, we did not have spatial working memory task data for all subjects. Thus, our functional localization relies on group-average spatial working memory results should be interpreted with caution.

### **Individual differences in DLPFC activation during spoken word recognition**

Because of the variability of outcomes in CI users (Firszt, Holden et al. 2004, Holden, Finley et al. 2013), one promising thought is that individual differences in brain activation may help explain variability in speech perception ability. Although our study was not powered for individual difference analysis (Yarkoni and Braver 2010), we conducted exploratory correlations to investigate this avenue of inquiry. Interestingly, we saw a trend such that poorer hearing in the left (non-CI) ear was correlated with increased activity in DLPFC. Our participants with CIs had significant variability in left ear hearing. Because the speech task was conducted using loudspeakers, we would expect both ears to contribute to accurate perception. Thus, poorer hearing in the left ear would create a greater acoustic challenge, with a correspondingly greater drain on cognitive resources. This interpretation will need additional data to be properly tested.

### **Conclusions**

Using high-density optical neuroimaging, we found increased activity in DLPFC in listeners with cochlear implants compared to listeners with normal hearing. Our findings are consistent with a greater reliance on domain-general cognitive processing and provide a potential framework for the effort that many CI users need to expend during speech perception, even in quiet.



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347 in our study.

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## Conflict of interest

349 The authors declare that the research was conducted in the absence of any commercial or  
350 financial relationships that could be construed as a potential conflict of interest.

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