Behavioral/Cognitive

Improved Speech Hearing in Noise with Invasive Electrical Brain Stimulation

Prachi Patel,1,2* Bahar Khalijhinejad,1,2* Jose L. Herrero,3,4 Stephan Bickel,3,4 ©Ashesh D. Mehta,3,4 and Nima Mesgarani1,2

1Mortimer B. Zuckerman Mind Brain Behavior Institute, Columbia University, New York, New York 10027, 2Department of Electrical Engineering, Columbia University, New York, New York 10027, 3Hofstra Northwell School of Medicine, New York, New York 11549, and 4Feinstein Institute for Medical Research, New York, New York 11030

Speech perception in noise is a challenging everyday task with which many listeners have difficulty. Here, we report a case in which electrical brain stimulation of implanted intracranial electrodes in the left planum temporale (PT) of a neurosurgical patient significantly and reliably improved subjective quality (up to 50%) and objective intelligibility (up to 97%) of speech in noise perception. Stimulation resulted in a selective enhancement of speech sounds compared with the background noises. The receptive fields of the PT sites whose stimulation improved speech perception were tuned to spectrally broad and rapidly changing sounds. Corticocortical evoked potential analysis revealed that the PT sites were located between the sites in Heschl’s gyrus and the superior temporal gyrus. Moreover, the discriminability of speech from nonspeech sounds increased in population neural responses from Heschl’s gyrus to the PT to the superior temporal gyrus sites. These findings causally implicate the PT in background noise suppression and may point to a novel potential neuroprosthetic solution to assist in the challenging task of speech perception in noise.

Key words: auditory cortex; human electrophysiology; speech perception

Significance Statement

Speech perception in noise remains a challenging task for many individuals. Here, we present a case in which the electrical brain stimulation of intracranially implanted electrodes in the planum temporale of a neurosurgical patient significantly improved both the subjective quality (up to 50%) and objective intelligibility (up to 97%) of speech perception in noise. Stimulation resulted in a selective enhancement of speech sounds compared with the background noises. Our local and network-level functional analyses placed the planum temporale sites in between the sites in the primary auditory areas in Heschl’s gyrus and nonprimary auditory areas in the superior temporal gyrus. These findings causally implicate planum temporale in acoustic scene analysis and suggest potential neuroprosthetic applications to assist hearing in noise.

Introduction

Speech communication often takes place in the presence of competing sound sources, yet we are able to carry on conversations effortlessly even when speech signals are mixed with considerable noise. The neural processes that enable the segregation and enhancement of the acoustic features of speech relative to background noise remain largely unknown (Bregman, 1994; Assmann and Summerfield, 2004). It has been shown that the invariance of speech emerges gradually as the neural responses to sound ascend in the auditory pathway from the cochlea (Wang and Shamma, 1994) to the thalamus (Miller et al., 2001) and primary and nonprimary cortical areas (Kumar et al., 2007; Hong et al., 2008; Rabinowitz et al., 2013; Mesgarani et al., 2014). Studies of speech-in-noise perception in humans have found an increasingly invariant cortical representation of speech in the nonprimary auditory cortex that is unaffected by noise (Kell and McDermott, 2019). This invariant representation is constructed by the selective suppression of the encoded noise features in neural responses that...
occur across multiple anatomic areas, including Heschl’s gyrus (HG), the planum temporale (PT), and the superior temporal gyrus (STG) (Khaliighinejad et al., 2019). The causal role of each of these regions in removing noise from speech is not yet fully understood; and in particular, the role of the PT in acoustic scene analysis remains debated (Hickok and Saberi, 2012).

Anatomical studies of the PT have shown that it is an intermediary area between HG and the STG (Griffiths and Warren, 2002; Morosan et al., 2005; Hickok and Saberi, 2012), placing its function between those of nonspecific responses to speech in HG and speech-specific responses in the lateral STG (Humphries et al., 2014). These findings are consistent with the functional studies that have speculated on the role of the PT in the separation and identification of sound sources from background sounds (Griffiths and Warren, 2004; Isenberg et al., 2012). Indeed, an increased cortical surface area in the PT has been shown to correlate with the accuracy of acoustically distorted speech sound categorization (Elmer et al., 2013), confirming the role of the PT as a primary processor of rapidly changing acoustic cues in speech and nonspeech signals (Meyer et al., 2012).

Beyond these correlational studies that suggest a role for the PT in processing speech in noise, the causal role of the PT in speech perception in noise has not yet been studied. This absence of progress is because of the lack of methods that can manipulate neural responses with a high degree of spatiotemporal specificity in awake behaving humans as they engage in realistic speech-in-noise perception tasks. One such method that is often used for clinical mapping is electrical brain stimulation (EBS). During EBS, an electrical charge is delivered to a focal brain area to disrupt its function (Parvizi and Kastner, 2018). EBS in humans is unique because humans can articulate their perceived experiences during stimulation, an advantage that is absent in animal models. In the auditory domain, previous studies have reported that EBS of the STG causes auditory hallucinations (e.g., hearing a buzzing sound), illusions, and errors (e.g., hearing a distorted version of a sound) (Selimbayoglu and Parvizi, 2010; Leonard et al., 2019), suppression of tinnitus (Fenoy et al., 2006), transient hearing loss (Sinha et al., 2005), and have implicated the posterior STG in basic auditory functions, such as syllable discrimination (Boatman et al., 1995; Miglioretti and Boatman, 2003). On the other hand, EBS of the medial HG can induce the perception of distinct tones (Donovan et al., 2015). The effect of EBS in PT remains less clear because of the limited intracranial studies with depth coverage to target this region. Notably, none of the previous EBS studies in the human auditory cortex has demonstrated a facilitative role for EBS in speech perception, a task that remains challenging, particularly in adverse and noisy acoustic conditions.

In this study, we used a unique instance in which an epilepsy patient was implanted with both grid and depth electrodes (intracranial EEG [iEEG]) covering multiple auditory areas, including HG, the PT, and the STG. We stimulated and recorded the responses of HG, the PT, and the STG during a speech-in-noise perception task. Stimulation of the PT sites resulted in significant improvement in both the perceived quality and intelligibility of speech. Furthermore, we showed distinct local- and network-level properties for these neural sites using spectrotemporal receptive field analysis, corticocortical evoked potentials (CCEPs), and speech-nonspeech discriminability. This study suggests that the PT has a causal role in speech-in-noise perception and suggests potential neuroprosthetic solutions to enhance speech-in-noise perception, which currently remain a major challenge for individuals with hearing loss.

### Materials and Methods

#### Experimental design and statistical analysis

**Participants and data collection**

A 27-year-old female adult with pharmacoresistant focal epilepsy was the subject of this study. The subject had self-reported normal hearing and showed no difficulty in speech communication during the neuropsychological language tests done before implant. The subject underwent chronic iEEG monitoring at North Shore University Hospital to identify epileptogenic focus in the brain for later removal. She was implanted with both surface grid & strip as well as depth electrodes (PMT). Electrodes showing any sign of abnormal epileptiform discharges, as identified in the epileptologists’ clinical reports, were excluded from the analysis. All included iEEG time series were manually inspected for signal quality and were free from interictal spikes. All research protocols were approved and monitored by the institutional review board at the Feinstein Institute for Medical Research, and informed written consent to participate in research studies was obtained from the subject before the implantation of electrodes.

**Stimulus**

The subject participated in four experiments: EBS, listening to continuous speech, listening to speech versus nonspeech sounds, and CCEPs. The details of each experiment are described below.

#### Experiment 1: EBS during speech-in-noise

Bipolar electrical stimulation was delivered to neighboring contacts along the shaft of a stereotactic high-density depth electrode (16 contacts, 2.2 mm intercontact distance, 1.3 mm contact size) using 200 μs squared-wave biphasic pulses at 50 Hz for 4 s (S12 stimulator, Grass Technologies). Two intensities (1 and 3 mA) were tested. The patient was asked to keep her eyes open during the procedure. We used a standard speech-in-noise intelligibility test (BKB-SIN) (Wilson et al., 2007) to measure the intelligibility of speech during stimulation of electrodes. The speech-in-noise sentences were sampled at 20,000 Hz.

Although every contact was stimulated at least once, the objective and subjective measurements of the sham versus stimulation trials were calculated based on 60 stimulation trials of one site along electrode shaft in the left PT (see Fig. 1B, electrode contact 8-9) because they had the highest noise reduction effect based on subject self-report. Randomized sham stimulations (asking the patient to report the percepts without introducing any current into the electrodes) were performed for the quantification of intelligibility and quality improvement. During the sham trials, we specifically tested the placebo effect by counting “1, 2, 3” before clicking the stimulator button, similar to how the stim trials were performed, but the electrical current was set at 0 mA. EEG and clinical signs in the patient ruled out the involvement of HG, the PT, and the STG in the patients’ seizures, and the patient was instructed to report whether the electrical stimulation caused her typical seizure auras. The patient did not report experiencing seizure auras during the experiment.

#### Experiment 2: listening to continuous speech stories

The subject listened to stories recorded by four voice actors (two males and two females) with a duration of 20 min and a sampling rate of 11,025 Hz. The sentences were on an average 5.2 s long with intersentence interval of 0.5 s. The stimuli were presented using a single Bose SoundLink Mini 2 speaker situated directly in front of the subject. The stimuli and the neural responses to these stimuli were used to calculate the spectrotemporal receptive fields of each neural site.

#### Experiment 3: listening to speech versus nonspeech sounds

The subject listened to 20 min of 69 commonly heard natural sounds. Among these 69 sounds were 16 samples of English and foreign speech and 53 nonspeech sounds from 14 categories (coughing, crying, screaming, music [jazz, pop, classical], animal vocalizations, laughing, syllables, sneezing, breathing, singing, shooting, tones, drumming, and subway noise) (Khaliighinejad et al., 2021). The sounds were on average 12.5 s long with intersentence interval of 0.5 s. To find the neural representation of each sound, we averaged the high γ (70-150 Hz) activity in response to
The interstimulation interval was 1.5 s (biphasic, 100 mV/phase, 30 trials per electrode pair) using a Grass S12 cortical stimulator. The SKT electrodes were used as references, as dictated by the recording quality at the bedside after online visualization of the spectrogram of the signal. Speech signals were recorded simultaneously with the iEEG for subsequent offline analysis. All further processing steps were performed offline. The iEEG data were resampled to 512 Hz. A first-order Butterworth high-pass filter with a cutoff frequency of 1 Hz was used to remove DC drift. Line noise at 60 Hz and its harmonics (up to 240 Hz) were removed using second-order IIR notch filters with a bandwidth of 1 Hz. The envelope of high γ activity, which correlates with neural firing in the proximity of the electrodes (Ray and Maunsell, 2011; Buzsáki et al., 2012), was used as a measure of the neural response. To obtain the envelope of this broadband signal, we first filtered the data into eight frequency bands between 70 and 150 Hz (Edwards et al., 2009). Then, the envelope of each band was obtained by taking the absolute value of the Hilbert transform. We took the average of all eight frequency bands as the final envelope. The data were resampled to 100 Hz for further analysis. Neural sites that were responsive to sound were determined by a permutation test between responses to silence and all sounds from Experiment 3 (t test, FDR-corrected, q < 0.01) (Benjamini and Yekutieli, 2001).

Video–iEEG monitoring demonstrated seizures with an onset at the medial and inferior temporal lobe. Frequent interictal spike and wave discharges were also observed in the posterior subtemporal regions. None of the electrodes in HG, the PT, or the STG were part of the irritative or seizure onset zones.

**Behavior quantification**

To evaluate the quality of speech sentences, we asked the subject to repeat the sentence that was played and rate its quality using the Mean Opinion Scale (MOS) scale (Salza et al., 1996). An MOS rating of between 1 and 5 (1 = bad; 2 = poor; 3 = fair; 4 = good; 5 = excellent) was given. Intelligibility was measured as the percentage of key words identified in presented sentences using the BKB–SIN test (Wilson et al., 2007).

To evaluate the perceived tone frequency when HG electrodes were stimulated, the subject was given a knob that varied the tone frequencies being played. The subject was asked to move the knob until the presented pitch matched the tone frequency she perceived when the HG electrode was stimulated.

**Preprocessing neural data**

iEEG signals were acquired continuously at 3 kHz per channel (16-bit precision, range ± 8 mV, DC) with a data acquisition module (Tucker-Davis Technologies). The skull electrodes were used as references, as dictated by the recording quality at the bedside after online visualization of the spectrogram of the signal. Speech signals were recorded simultaneously with the iEEG for subsequent offline analysis. All further processing steps were performed offline. The iEEG data were resampled to 512 Hz. A first-order Butterworth high-pass filter with a cutoff frequency of 1 Hz was used to remove DC drift. Line noise at 60 Hz and its harmonics (up to 240 Hz) were removed using second-order IIR notch filters with a bandwidth of 1 Hz. The envelope of high γ activity, which correlates with neural firing in the proximity of the electrodes (Ray and Maunsell, 2011; Buzsáki et al., 2012), was used as a measure of the neural response. To obtain the envelope of this broadband signal, we first filtered the data into eight frequency bands between 70 and 150 Hz (Edwards et al., 2009). Then, the envelope of each band was obtained by taking the absolute value of the Hilbert transform. We took the average of all eight frequency bands as the final envelope. The data were resampled to 100 Hz for further analysis. Neural sites that were responsive to sound were determined by a permutation test between responses to silence and all sounds from Experiment 3 (t test, FDR-corrected, q < 0.01) (Benjamini and Yekutieli, 2001).

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output of the filter bank was then resampled to 16 frequency bands to prevent parameter overfitting. The amplitude of the high γ band was used as the measure of neural activity. Regularization and sparseness parameters were found via cross-validation (David et al., 2007). The best frequency and response latency parameters were estimated by finding the center of the excitatory region of the STRF along the frequency and time dimensions.

Multidimensional scaling (MDS) analysis
To calculate the MDS diagram of speech and nonspeech sounds, we first found the average of the high γ activity across the duration of the sounds in each category. In determining these averages, we eliminated the small segments of silences during the trial by averaging only the samples with above-threshold spectrogram energy. Next, we calculated the Euclidean distance between the average response to different sounds to find a dissimilarity matrix. To visualize this dissimilarity matrix, we used a two-dimensional MDS algorithm based on Kruskal’s normalized criterion to minimize stress for the two MDS dimensions (Cox and Cox, 2008).

Analysis of CCEPs
CCEP mapping was performed with bipolar stimulation of each pair of adjacent electrodes with single pulses of electrical current (10 mA, biphasic, 100 μs/phase, 30 trials per electrode pair) using a Grass SI2 cortical stimulator (Grass Technologies). Electrical stimulation artifact was found in first 20 ms of the data. This artifact was removed from each CCEP before analysis. Recorded neural data were sampled at 3000 Hz and bandpass filtered at 0.1-1 kHz. Acquired data were notch filtered at 60 Hz. The interstimulation interval was 1.5 s (±0.5 s). Differences in the interstimulation interval had no effect on evoked potentials. A current magnitude of 10 mA was chosen for grid/strip electrodes and 4 mA for depth electrodes. CCEPs in the human cortex generally consist of an early sharp response (10-50 ms poststimulation) and a later slow wave (50-250 ms). However, it has been shown that polarity can be positive in early sharp response (10-50 ms poststimulation) and a later slow wave (50-250 ms). It has been shown that polarity can be positive in early sharp response (10-50 ms poststimulation) and a later slow wave (50-250 ms). It has been shown that polarity can be positive in early sharp response (10-50 ms poststimulation) and a later slow wave (50-250 ms).

Measurement of improved intelligibility and quality of perceived speech after EBS of the PT electrode
We systematically tested the behavioral effect observed during clinical stimulation while the subject listened to speech in noise sentences (see Materials and Methods). Half of the trials were chosen randomly for stimulation (stim trials), and the other half were performed with no stimulation (sham trials) (Fig. 1C). The patient was asked to repeat the sentence and rate its quality using the MOS scale from 1 (poor) to 5 (excellent) (Salza et al., 1996) (see Materials and Methods). The reported MOS scale was used as the measure of perceived quality of speech, and the percentage of correctly repeated key words was used as the measure of perceived intelligibility of speech (Wilson et al., 2007).

We tested four different conditions (Fig. 1D). In Condition 1, we used jet background noise; in Conditions 2, 3, and 4, we used bar background noise. In Condition 4, we reduced the stimulation current from 3 to 1 mA (Fig. 1D). In Condition 1, where the background noise was jet noise with a signal-to-noise ratio (SNR) of −2.27 dB, the patient rated the speech quality significantly higher in the stim trials than in the sham trials (MOS = 3.2 vs 2.4, p < 10−3, N = 24, Wilcoxon rank-sum test). In addition, speech intelligibility was significantly higher in the stimulated jet noise condition than in the sham trials (91% correct vs 46% correct, p < 0.005, N = 24, Wilcoxon rank-sum test).

In Condition 2, where the background noise was bar noise with an SNR of −2.9 dB, the patient rated the speech quality significantly higher in the stim trials than in the sham trials (3.7 vs 3.1, p = 0.02, N = 36, Wilcoxon rank-sum test). However, we did not find a significant difference between the intelligibility of speech in the stim trials compared with the sham trials (67% correct vs 65% correct, p = 0.9 [not significant], N = 36, Wilcoxon rank-sum test).

In Condition 3, we tested the effect of stimulation in speech in noise with a high SNR, where the background noise was bar noise with an SNR of 3 dB. All of the sentences in this high-SNR condition were intelligible with or without stimulation. However, the perceived quality of the speech was significantly higher in the stim trials than in the sham trials (4.5 vs 3, p < 10−3, N = 41, Wilcoxon rank-sum test).

In Condition 4, as a control condition, we reduced the stimulation current to 1 from 3 mA (with bar background noise and an SNR of −4 dB). We observed that stimulation at a lower current (1 mA) did not result in improvement in the perceived quality of speech, although the patient could detect that a lower condition was present.
**Table 1. The full subjective report of the stimulation experiment**

| Patient describing the denoising effect of stimulation: |
|----------------------------------------------------------|
| - I heard the noise when it started, and as soon as you did whatever you did, all I heard was his voice. |
| - The voices get a lot clearer; I still hear the noise, but the voice gets a lot clearer, as if someone is saying it in my ear. I still hear the background, but the voice is louder, more prominent. |
| - It is always the speech that gets stronger; it's never the background noise. The person's voice becomes more prominent over the background noise, as if someone gives that person a microphone. Kind of like they tell everyone to hush, to turn their background noise down and let this person talk. When you are both talking, I hear you both just as clear; it is just the noise. If two people talk at the same time, they both increase in strength; it's just the background noise. |
| - The easiest way for me to explain it is when you take an equalizer for music and you change the different modes of how you want to hear the music; that's how. |

**Patient describing the time-varying nature of the denoising effect:**

- I heard “snow falls” clearly, and there were two more words, but I didn’t hear the two words. I heard “snow falls” at approximately 5 (excellent), and then after that, I didn’t hear the two other words. I just feel that it all blended in as the background noise came back. |
- I heard [the first word] and I felt that something happened, but the quality started to fade. It was first at 4 (good), and then I heard up to [five], and then I didn’t hear anything afterward.

- It is like I hear the voice clearly, and then everything else just comes back along with it, background noise and voices. As soon as he started talking, I heard those first two words clearly with no background noise, (without) anything, and then after the word “old,” everything just came back all at once. |
- It was a 4 (good) up to the word “mailman dropped,” and then I couldn’t understand anything after that. It was 2 (poor) after that because all the background noises came back. Half of it (the sentence) was clear; the first half (of the sentence) was clear. |

**Patient describing the stimulation effect:**

- I can feel kind of like popping in my ear — not a very strong popping, but I can feel change. Like I can feel that something got a bit clearer. |
- 1 mA vs 3 mA: A lot less strong. Things still got clearer, but not as strong.
- Not feeling it as strong as I heard it before. Still feel it, but less.

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Stimulation current was being used (p = 0.57, Wilcoxon rank-sum test).

**Description of the patient’s experience during stimulation**

Subjective reports of the effects of electrical stimulation are shown in Table 1 (see also Movie 1). Stimulation of electrode contacts 8-9 in the PT caused the patient to experience a complex auditory effect: she reported improved quality and intelligibility of speech in background noise. In her own words, “The voices get a lot more clear; I still hear the noise, but the voice gets a lot more clear”; “It is always the speech that goes stronger; it’s never the background noise”; “If two people talk at the same time, they both increase; it only happens for the background noise”; and “[It’s] as if you take an equalizer for music and change the mode of how you want to hear it.” In Table 1, the patient’s description of 1 versus 3 mA stimulation is also included; she could feel the stimulation in both cases, but only the 3 mA stimulation caused the noise reduction effect.

**PT sites have distinct spectrotemporal tuning properties**

To examine the functional properties of the cortical sites and calculate their temporal and spectral tuning, we calculated the STRF of each electrode. The subject listened to 30 min of clean speech stories without the application of any electrical stimulation. The envelope of the high frequency band (70-150 Hz), which correlates with neural firing in the proximity of the electrode (Ray and Maunsell, 2011; Buzsáki et al., 2012), was extracted as the neural response measure of the recorded signals (see Materials and Methods). We found that the electrodes in HG were narrowly tuned to a specific frequency range (Fig. 2A); on the other hand, the electrodes in the PT were responsive to temporal changes across a broad range of frequencies, as shown in Figure 2B.

It is worth mentioning that we accurately measured the frequency of the hallucinated tone in HG by asking the subject to manually adjust the frequency of a tone generator to the frequency of the induced tone. We did not find any relationship between the best frequency of the contacts in HG and the frequency that was induced through stimulation. Specifically, the subject heard 230, 230, 250, and 250 Hz as a result of stimulation.
Functional connectivity of HG and the STG through the PT

Stimulation of a neural site affects not only the site where the current is directed but also the network of regions that are connected to it. To examine the spatial extent of the stimulation and to test the differences in connectivity of the cortical sites located in HG and the STG versus the PT and the STG, we used the CCEP method. CCEP mapping applies single pulses of a current to measure electrophysiological responses with accurate localization and evaluate interareal connectivity (Keller et al., 2014a, 2018).

Most CCEPs consist of an early (10-30 ms) negative surface deflection labeled N1 and a later (80-250 ms) slow wave labeled N2. Although studies have shown a possibility of shorter N1 component at 1.7 and 2.3 ms (Brugge et al., 2003), the N1 of CCEPs from our study align with the 10-30 ms shown by Keller et al. (2014a). The N1 and N2 components of CCEPs exist across spatially diverse recording sites after stimulation. Therefore, the stimulation-evoked response provides a measure of directional connectivity that is calculated directly from the cortical areas with high spatial resolution. It has been shown that the number of white matter tracts measured with DTI is positively correlated with the strength of the N1 component of CCEPs (Keller et al., 2014a,b, 2018).

We divided the speech-responsive sites in this subject into three groups based on their anatomic locations: the HG, the PT, and the STG. We tested the connectivity among the sites in HG, the PT, and the STG (Fig. 3A). To test whether connectivity between the PT and the STG differs from connectivity between HG and the STG, we examined the N1 component of the evoked responses in the STG induced by stimulation of the PT versus stimulation of HG sites. We observed that the stimulation of electrodes in the PT, but not HG, resulted in a significantly stronger N1 in electrodes responsive to speech in the STG. In Figure 3B, representative evoked potentials for individual electrodes are shown. The N1 component induced by stimulation of the PT compared with stimulation of the HG was significantly stronger in recorded neural sites in the STG (20.45 ± 0.6 vs 5.7 ± 0.42 μV, t test, p < 0.001; Fig. 3C).

We generated an adjacency matrix and digraphs to express the connectivity of the neural sites (Biggs et al., 1993). The adjacency matrix of a graph is a square matrix in which the elements of four contacts in HG with optimal frequencies of 715, 676, 684, and 963 Hz (see Materials and Methods).

Figure 3. CCEP activity in the STG through stimulation in PT versus HG. A, Location of electrodes in the HG, the PT, and the STG. B, Evoked responses in representative sites in the HG, in the PT, and in the STG using corticocortical stimulation of the HG versus the PT. Bottom row represents the average of the absolute value of the evoked responses for all neural sites in three areas (HG, PT, and STG). C, Comparison of the absolute value of amplitude of N1 recorded in the STG and generated by stimulation of the PT versus HG.
indicate the distance between each pair of nodes. From this adjacency matrix, we can generate a digraph (Gross and Yellen, 2005), which is a directed graph of the connectivity between the nodes, with edge arrows showing the direction of the connection and the relative location of nodes showing the strength of connectivity. From the previous analysis, we obtained the CCEPs between two electrodes and normalized their mean and variance based on the neural response before the start of the stimulation. We calculated the absolute value of the N1 component of this normalized CCEP between two electrodes to fill in the elements of the adjacency matrix as a measure of connectivity (rows indicate the stimulated electrode, and columns indicate the target electrode where the CCEP was measured). Thus, each element of this matrix gives a measure of connectivity between the respective electrodes. We further applied a threshold to the adjacency matrix by assigning a value of 1 for significant connections and a value of 0 for nonsignificant connections (see Materials and Methods). Using this adjacency matrix, we generated directional digraph plots with nodes indicating electrodes, edges with arrows indicating the direction of connectivity between the nodes, and the location of nodes based on the method of force-based graph drawing (Fruchterman and Reingold, 1991). In this method, nodes that are not connected are placed further apart in the graph, and those that are highly connected are placed close together in the graph (see Materials and Methods; Fig. 4A). This analysis revealed an overall pattern in which the electrodes in HG, the PT, and the STG were placed closer to the electrodes in the STG than to the electrodes in HG. It is important to note that our analysis of the network properties is limited to the electrodes from which we were recording and does not represent all parts of HG or the PT.

The observed intermediate location of the PT is also supported by the results of a response latency analysis (see Materials and Methods). We first calculated the latency of each neural site and averaged the values in each area, as shown in Figure 5. This figure shows that response latency gradually increases from HG to the PT to the STG. The latency of the response along the auditory pathway approximately reflects the number of synapses away from the auditory periphery and hence has been used to speculate the direction of information processing in the auditory cortex (Da Costa et al., 2011; McMurray and Jongman, 2011; Nourski et al., 2014).

**Separation of speech and noise starts in the PT**

In addition to latency, we also looked at the separation of speech from nonspeech sounds in each region. Neural responses to specific categories of sounds, such as speech versus nonspeech sounds, have been attributed to a higher level of neural processing in the auditory cortex (Chan et al., 2014). To examine the neural responses to speech versus nonspeech sounds, we designed a task that consisted of 69 samples of sounds: 16 of the sounds were English and foreign news segments, and 53 were diverse sounds, such as coughing, crying, screaming, noise, music, animal vocalization, laughing, singing, shooting, and
drumming. We determined the separability of the responses to speech versus nonspeech category of sounds using unpaired \( t \) test. We observed that the segregation of speech from nonspeech sounds gradually increased from the HG to the PT to the STG (Fig. 6A). To better demonstrate how the separation of speech and nonspeech sounds takes place along these regions, we projected the response of sites in each region onto a two-dimensional MDS diagram (see Materials and Methods). Figure 6B shows that, while the responses to speech and nonspeech sounds fully overlap in HG, they begin to form separate categories in the PT and become fully separate in the STG.

Our characterization of the electrodes located in HG and the PT and STG can be summarized as follows: (1) CCEP analysis showed that the PT electrodes are situated between the HG and STG electrodes; (2) response latency increases from the HG electrodes to PT electrodes to the STG electrodes; and (3) the responses to speech and nonspeech sounds becomes more distinct from the HG to the PT to the STG electrodes. Collectively, these results suggest that our electrodes in the PT are located between the electrodes in the HG and the STG. This intermediate location might explain the perceptual effect generated by stimulating the electrodes in this region, which is absent during the stimulation of electrodes in HG and the STG.

**Discussion**

We report that EBS of electrodes implanted in the PT in one patient significantly and reliably improved both the perceived quality and the intelligibility of speech in noise. The subject reported the suppression of background noise and the selective amplification of speech sounds. We observed significant improvement in both the subjective quality rating and the objective intelligibility score of speech in background noise. The neural sites whose stimulation resulted in enhanced perception of speech had distinct properties compared with the sites in HG; namely, their receptive fields were more tuned to rapid temporal changes in spectrally broad sounds and had a longer response latency. Moreover, network CCEP and speech/nonspeech separability analysis revealed an intermediary role of the neural sites in the PT, suggesting an intermediate functional role relative to the sites in HG and the STG.

Our results causally implicate the examined neural sites in the PT in the suppression of background noise. This triangular region, which occupies the superior temporal plane posterior to HG, is believed to be part of the auditory association cortex (Hickok and Poeppel, 2007). The PT has been suggested to play a role in auditory scene analysis because of its modular structure and multimodal and diverse patterns of neural processing (Griffiths and Warren, 2002). For example, studies have shown that portions of the PT selectively respond to spatial sounds, including moving sounds (Warren et al., 2002; Warren and Griffiths, 2003), with the anterior PT showing sensitivity to pitch-related acoustic changes and the posterior PT showing sensitivity to changes in spatial location (Warren and Griffiths, 2003). Other studies have shown that, in addition to this pure acoustic feature selectivity, the PT is sensitive to spatial sound source locations only when the location serves as a cue for auditory object disambiguation, as opposed to being purely selective of spatial features (Zatorre et al., 2002). Similarly, one study showed that no subregion of the PT was explicitly selective of spatial or object-related information; instead, the PT actively processes spatial cues to aid auditory stream segregation (Smith et al., 2010). Hence, a task/goal-based role of the PT in auditory stream segregation and integration has emerged (Ragert et al., 2014). Consistent with this view, our study is the first to provide experimental evidence in support of an active and causal role of the PT in the crucial task of separating speech from background noise. Moreover, we found that the receptive fields of the PT are distinctly more sensitive to broad spectral temporal changes than the sites in HG. This is in line with anatomic studies showing that the neurite architecture of the PT increases its temporal precision and thus facilitates the processing of auditory speech (Ocklenburg et al., 2018) and with functional studies showing the role of the PT in integrating sequential auditory events (Mustovic et al., 2003). This functional characteristic of the PT may be crucial in auditory scene analysis and noise suppression, as speech and most background noises differ substantially in the spectrotemporal domain (Mesgarani et al., 2006; Mesgarani and Shamma, 2007).

EBS is regarded as complementary to methods that study the neural correlates of stimuli and behavior because EBS directly tests the causal relationship between brain regions and perception. The efficacy of EBS has been demonstrated in vision and memory tasks (Jacobs et al., 2012; Parvizi et al., 2012; Mégevand et al., 2014; Keller et al., 2017; Schalk et al., 2017). Many previous EBS studies relied solely on qualitative descriptions of the subject’s experience (Parvizi et al., 2012; Mégevand et al., 2014; Schalk et al., 2017). In contrast, we supplemented the subject’s qualitative report with additional quantitative measures to determine the statistical significance of the perceived effects compared with the control (sham) condition. Previous studies of clinical language-mapping protocols used to guide neurosurgical
resections have commonly shown the induction of transient language deficits (Borchers et al., 2012). These clinical mapping studies have identified sites that are critical for the perception and discrimination of speech and other complex sounds in the posterior temporal lobe, corresponding to the auditory association cortex (Boatman et al., 1995; Boatman and Miglioretti, 2005), by showing that EBS of the posterior STG causes selective suppression of speech over nonspeech sounds (Sinai et al., 2009). However, to our knowledge, the improvement of speech perception following direct brain stimulation has no precedence in the prior literature. Notably, noninvasive transcranial brain stimulation has also been shown to enhance auditory responses in EEG (Van Doren et al., 2014), improve auditory gap-detection performance (Rufener et al., 2017), bias attention in a spatial multitalker task (Wöbstmann et al., 2017), and improve speech perception in cocktail party scenarios (Riecke et al., 2018). Compared with these noninvasive studies, invasive and direct EBS has the power to target a specific brain region, which can result in large and reproducible behavioral effects at the single-trial level, such as those we reported in this study.

Determining how EBS changes neural representation and computation is not a trivial endeavor. It is challenging because of the uncertainty of the spatial extent of the cortex that is responsive to stimulation and the relationship between the circuitry engaged by EBS and the types of neural responses elicited by sensory stimulation. EBS of similar sites in different patients has been shown to yield different results (Borchers et al., 2012; Desmurget et al., 2013). First, small differences in electrode position lead to large differences in targeted responsive neurons (Histed et al., 2009); second, the location of brain functions varies among individual patients (Borchers et al., 2012); and finally, these networks are susceptible to reorganization (Enatsu et al., 2013). Furthermore, EBS can generate complex behavioral effects in regions that are involved in neural processing (Fried et al., 1998; Desmurget et al., 2009; Parviz et al., 2013). Similar to these studies, we found a specific behavioral effect, although the stimulation signal itself was generic and nonspecific. Additionally, whether EBS of a brain area results in the suppression of or an increase of neural activity is still a matter of scientific debate (SelimBayoglu and Parviz, 2010). Extensive preclinical studies have shown that high-frequency (~100 Hz) EBS increases neuronal excitability (Bliss and Lømo, 1973; Douglas, 1977; Skrede and Malthe-Sørenssen, 1981), whereas low-frequency stimulation (~1 Hz) decreases neuronal excitability (Mulkey and Malenka, 1992). As a result, several questions warrant further research, including the characterization of local and remote effects of EBS, its inhibitory and excitatory effects (Borchers et al., 2012).

Our study cannot adequately answer how the stimulation of electrodes in the PT results in a perceived reduction in noise. One possible explanation is motivated by our observation of a gradual separation of speech and noise encoding along the auditory pathway (Bar-Yosef and Nelken, 2007; Norman-Haignere et al., 2015). Given these findings, it is possible that the partially separated representations of speech and noise may be differentially targeted by electrical stimulation and hence may be selectively enhanced or suppressed. Consistent with this hypothesis, we found that the representation of speech and noise at PT sites was more separable than the representations at HG sites but less separable than those at STG sites. Additionally, our analysis of latency and network connectivity (CCEP) placed the PT sites between the HG and STG sites. It is plausible that selective suppression of the neural representation of background noise in the PT could reduce its perception. Alternatively, stimulation can activate and excite recurrent connections to upstream and downstream areas that may engage inhibitory connections and hence result in the increased removal of noise from the mixed sound. While we cannot determine the neural mechanism underlying this perceptual effect, future research that allows a better understanding of the role of EBS can result in a more conclusive explanation of the behavioral effect reported in this study and advance our knowledge of the role of the PT in speech-in-noise perception. Finally, speech perception in noise is a very challenging task for individuals with hearing loss. This study opens the possibility of neuroprosthetic solutions that can directly manipulate the cortical representation of speech to enhance the perception of a target sound among competing sources, which can assist individuals who struggle to hear speech in adverse acoustic conditions.

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