

Direct cortical stimulation of inferior frontal cortex disrupts both speech and music production in highly trained musicians

Matthew K. Leonard^a, Maansi Desai^a, Dylan Hungate^a, Ruofan Cai^a, Nilika S. Singhal^b, Robert C. Knowlton^b, & Edward F. Chang^{a*}

^aDepartment of Neurological Surgery, University of California, San Francisco, 505 Parnassus Ave., San Francisco, CA 94143, USA

^bDepartment of Neurology, University of California, San Francisco, 505 Parnassus Ave., San Francisco, CA 94143, USA

* Corresponding author. Department of Neurological Surgery, UCSF Medical Center, 513 Parnassus Avenue, HSE 821, San Francisco, CA, 94143. Email: Edward.Chang@ucsf.edu

Author Email Addresses:

Matthew K. Leonard: Matthew.Leonard@ucsf.edu

Maansi Desai: Maansi.Desai@ucsf.edu

Dylan Hungate: Dylan.hungate11@gmail.com

Ruofan Cai: rfcai@uw.edu

Nilika S. Singhal: Nilika.Singhal@ucsf.edu

Robert C. Knowlton: Robert.Knowlton@ucsf.edu

Edward F. Chang: Edward.Chang@ucsf.edu

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Music and speech are human-specific behaviors that share numerous properties, including the fine motor skills required to produce them with the vocal tract or manual articulators. Given these similarities, previous work has suggested that music and speech may at least partially share neural substrates. To date, much of this work has focused on perception, and therefore has not investigated the neural basis of production, particularly in individuals who are highly trained musicians. Here, we report two rare cases of musicians undergoing neurosurgical procedures, where it was possible to directly stimulate the cortical surface in a variety of left hemisphere brain regions during speech and piano/guitar music production tasks. We found that stimulation to left inferior frontal cortex, including pars opercularis and ventral pre-central gyrus, caused slowing and arrest for both speech and music, and note sequence errors for music. In contrast, stimulation to posterior superior temporal cortex only caused production errors during speech tasks. These results demonstrate dissociable networks underlying speech and music production, with a shared substrate in frontal regions that are typically thought to be specialized for speech and the vocal tract articulators.

Keywords: electrocortical stimulation; speech production; music; neurosurgery; language mapping

1. Introduction

Music and speech are uniquely human behaviors that are both characterized by complex sequences of motor actions with dynamic acoustic consequences. The extent to which neural representations of speech and music are separate or shared has been a topic of debate for many decades (Koelsch, 2011; LaCroix, Diaz, & Rogalsky, 2015; Patel, 2010; Zatorre, Belin, & Penhune, 2002). Whereas there may be differences in auditory regions like the superior temporal gyrus (STG; (Garcea et al., 2017; Katlowitz, Oya, Howard, Greenlee, & Long, 2017), particularly during perception (Norman-Haignere, Kanwisher, & McDermott, 2015; Zatorre et al., 2002), there is increasing

evidence for shared representations in prefrontal regions like BA44 (pars opercularis) in the inferior frontal gyrus (IFG; (Fadiga, Craighero, & D'Ausilio, 2009; LaCroix et al., 2015; Maess, Koelsch, Gunter, & Friederici, 2001; Özdemir, Norton, & Schlaug, 2006). To date, there have been only limited studies investigating the shared direct roles of left hemisphere core language network regions in music and speech production (Riva, Casarotti, Comi, Pessina, & Bello, 2016), thus it remains unknown whether areas like left STG, pars opercularis, and ventral sensorimotor cortex (vSMC) are necessary for both behaviors.

To address this question, we used direct electrocortical stimulation (ECS) mapping in two neurosurgical patients who were accomplished musicians. We applied current to the cortical surface of left frontal and temporal regions while these individuals performed a series of speech and music production tasks. Errors evoked by stimulation during the music tasks were compared with a standard clinical battery of speech tasks, which included both exogenous stimulus-driven (e.g., repetition, picture naming, auditory naming) and endogenous internally-generated (e.g., numerical counting) behaviors. We were specifically interested in comparing both core language functions and more automatic sequential behaviors to the internally-generated production of highly familiar music. By examining the specific patterns of errors induced by stimulation to these regions, we demonstrate in these two rare cases that whereas left pars opercularis and vSMC are critical for producing spoken and musical sequences (regardless of whether the articulators are the vocal tract or the hands), left STG is critical only for speaking.

2. Materials/Methods

2.1 Participants

Patient 1 was a 16-year old, right-handed male with medically refractory epilepsy. He had experienced seizures since age 4, and treatment with anti-epileptic drugs was unsuccessful in managing the frequency and severity of the seizures. Thus, he was a candidate for intracranial monitoring in the pediatric epilepsy unit. During the monitoring period, he participated in ECS mapping procedures, done at the bedside.

Patient 2 was a right-handed male with a left insular low grade astrocytoma with new onset seizures. At age 25, he underwent surgery to resect the tumor. 23 months later, he underwent a second surgery to resect the regrowth of the tumor. During both intraoperative cases, he participated in awake cortical language mapping, and also played guitar to identify sites that disrupted his ability to perform music.

The study was approved by the UCSF Committee for Human Resource Protection Program. Cortical stimulation was conducted for clinical purposes. The participants (and legal guardians in the case of Patient 1) gave written informed consent to participate in the experiments prior to surgery.

2.2 Procedures

Patient 1 was an accomplished classical musician and in addition to undergoing standard language mapping procedures, he requested prior to surgery to preserve his musical abilities. We worked with him in the months leading up to his surgery to custom design a testing protocol that could be used to ensure resection of the seizure focus did not impair either his language or his musical abilities. Patient 1 specifically learned a piano piece before surgery so that he could perform it during clinical stimulation mapping and electrocorticographic (ECoG) recording (see (Martin et al., 2017) for a report on ECoG activity during music production).

To identify the cortical localization of speech and music, we asked Patient 1 to perform five tasks while stimulation was delivered to adjacent bipolar electrode pairs from the implanted electrode arrays. We used four standard clinical stimulation tasks to identify cortical sites that are critical for language: (1) *Repetition*, where the participant heard a set of four syllable words (e.g., “microscopic”) and was asked to repeat them aloud (similar procedures described in (Leonard, Cai, Babiak, Ren, & Chang, 2016)); (2) *Picture naming*, where the participant viewed line drawings of objects and was asked to name the images aloud; (3) *Auditory naming*, where the participant heard a description of an object (e.g., “a small flying bug that leaves an itchy bite”) and was asked to name the object (e.g., “mosquito”); and (4) *Counting*, where the participant was asked to count slowly in increasing order from one to thirty, or until instructed to stop.

Patient 1 also performed a task where a full-size electronic keyboard was mounted above the hospital bed. He played the Prelude No. 1 in C Major from the Well-Tempered Clavier Book I by Johann Sebastian Bach several times, as well as standard major scales. Several pieces were performed through the experiment, however only the Bach Prelude and scales were used for analysis as he was highly familiar with them prior to his admission, and was able to play them effortlessly. He was instructed to play the piece all the way through once, attempting to continue despite any stimulation-induced errors.

During all five tasks, current was delivered to pairs of electrodes on the implanted ECoG grid. Before the experiments, the clinicians determined which sites on the ECoG grid they would stimulate during each task, targeting motor and auditory regions. Each site was tested between 1 and 18 times (mean = 2.48, median = 2.0, std = 2.56) until at least one of three criteria was met: 1) the patient produced an error that

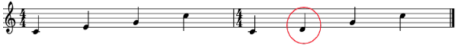


was synchronous with stimulation, 2) after-discharges were observed on the ECoG recordings, indicating that stimulation affected neural activity at the site, or 3) a maximum current amplitude of 6mA was reached and neither behavioral errors nor after-discharges were observed.

Patient 2 was an accomplished guitarist and like Patient 1, he requested that the resection not interfere with his musical abilities. During an awake craniotomy surgery, an Ojemann bipolar cortical stimulator (Integra LifeSciences, Plainsboro, NJ) with typical settings for mapping (60 Hz, bipolar, biphasic, 1ms pulse width) was used to perform intraoperative ECS at a variety of sites in sensorimotor and pre-frontal cortex (Breshears, Molinaro, & Chang, 2015; Chang et al., 2017). He performed the same four standard clinical language mapping procedures, and additionally strummed chords on a guitar. For the purposes of this report, only the counting task was studied in detail, as these data overlapped with regions stimulated during the music task.

2.3 Error Analysis

For each task, stimulation-induced errors were identified and characterized according to three phonological categories (substitution, deletion, addition), and two motor categories (slowing, arrest). These error types are described in **Table 1**, and are based on previously published methods (Leonard, Cai, et al., 2016).

Table 1: Error categories, coding criteria, and examples.

Error Category	Error Sub-type	Criteria	Example
Phonological	Substitution	Correct number of phonemes/notes, but production of an incorrect phoneme/note	<p>ɪntərdʒekʃən/ -> ɛntərdʒekʃən</p> 
	Deletion	Missing phoneme/note	<p>ɒləkəsi/ -> /ɛləkətsi</p> 
	Addition	Extra phoneme/note	<p>Broken Window → brok um broken... wɪndəʊ</p> 
Motor	Slowing	Phonologically/musically correct, but produced at a slower pace	“Prosperity” -> “pro---sper---ity”
	Arrest	Complete halting of production	[no production during stimulation]

Video files from both the speech and music tasks were extracted from the clinical ECoG monitoring system and every trial was hand-annotated and transcribed by

two of the authors (D.H. and M.D.) using ELAN (ELAN 2017). Both annotators viewed each video from Patient 1's clinical mapping and annotated instances in which errors occurred. Both annotators were initially blinded to when stimulation occurred. Next, the precise timing of stimulation was determined from the recorded ECoG signals, which showed clear stimulation artifacts. The two annotators independently reviewed the videos, and the separate results were then considered. When there was a disagreement between the two annotators for a particular error, a third annotator evaluated the video, the disagreement was discussed to resolve any discrepancies, and only errors on which there was agreement were included in the final analyses.

Error types were identified on a per-syllable basis for speech tasks and on a per-note basis for the music task. Error categories for the music task were analogous to the speech task as in the following examples (**Table 1**): (1) *Substitutions* were marked if a "C" was replaced by a "G"; (2) *Deletions* were marked if a particular note of a sequence was omitted ("C-D-E" -> "C-E"); (3) *Additions* were marked if a note was inserted within a sequence ("C-D-E" -> "C-D-D-E"); (4) *Slowing* errors were identified when the tempo of a particular passage slowed down during stimulation and then regained its original tempo after the end of the stimulation train; and (5) *Arrest* errors were marked when the participant stopped midway through a musical sequence or was unable to continue playing the sequence. For both speech and music tasks, only errors that occurred within 5 seconds of stimulation onset were used for the analysis (each stimulation event lasted 3 seconds).

For each site, task, and error type, the total number of errors and total number of stimulations were counted, and percent error rates were plotted on a 3D MRI reconstruction of the patient's brain. The electrode locations were determined from a post-operative computed tomography (CT) scan, which was co-registered to the

patient's preoperative structural magnetic resonance image (MRI) (Hamilton, Chang, Lee, & Chang, In Press). Electrode locations were manually checked and verified to ensure accurate locations and anatomical labeling. For plotting purposes, the stimulation site was marked as the Euclidean mid-point between the two electrodes in each bipolar pair.

2.4 Statistical Analysis

To evaluate error patterns statistically, we compared the observed errors to a shuffled distribution. Within each task, error rates were randomly shuffled across sites 1000 times to generate a null distribution. We then computed 95% confidence intervals for these distributions and compared the observed error rates to determine whether the errors at each site were above the upper bound of the 95% confidence interval for each site.

3. Results

Sites throughout peri-Sylvian cortex were tested during four speech tasks for Patient 1: repetition, picture naming, auditory naming, and counting. Stimulation during each speech task resulted in spatially separable error types. First, we examined which sites were associated with five distinct error types for each speech task (**Table 1**). The results are summarized in **Table 2** and **Figures 1 and 2**. All reported results were statistically robust, with error rates at each site in each task falling outside the 95% confidence interval of the randomly shuffled null distributions (see Methods).

Table 2: Summary of stimulation across anatomical regions in Patient 1. Data are collapsed across tasks and regions were defined by the Freesurfer anatomical atlas. “M” refers to errors on the music task, and “S” refers to errors on the speech tasks.

	Temporal			Frontal			Parietal
	<i>STG</i>	<i>MTG</i>	<i>ITG</i>	<i>IFG</i>	<i>Pre-central</i>	<i>Post-central</i>	<i>SMG</i>
Substitution	n=2 3.4% (M: 0) (S: 2)	n=0 --	n=0 --	n=2 15.4% (M: 2) (S: 0)	n=1 2.9% (M: 1) (S: 0)	n=0 --	n=0 --
Deletion	n=1 1.7% (M: 0) (S: 1)	n=0 --	n=0 --	n=0 --	n=1 2.9% (M: 1) (S: 0)	n=0 --	n=0 --
Addition	n=1 1.7% (M: 0) (S: 1)	n=0 --	n=0 --	n=0 --	n=3 8.6% (M: 3) (S: 0)	n=0 --	n=0 --
Slowing	n=4 6.8% (M: 0) (S: 4)	n=0 --	n=1 100% (M: 0) (S: 1)	n=3 23.1% (M: 1) (S: 2)	n=10 28.6% (M: 8) (S: 2)	n=0 --	n=0 --
Arrest	n=5 8.5% (M: 0) (S: 5)	n=0 --	n=0 --	n=0 --	n=7 20.0% (M: 3) (S: 4)	n=0 --	n=0 --
Total Errors	13 (M: 0)	0 (M: 0)	1 (M: 0)	5 (M: 3)	22 (M: 16)	0	0

	(S: 13)	(S: 0)	(S: 1)	(S: 2)	(S: 6)		
Total Trials	59	16	1	13	35	7	4

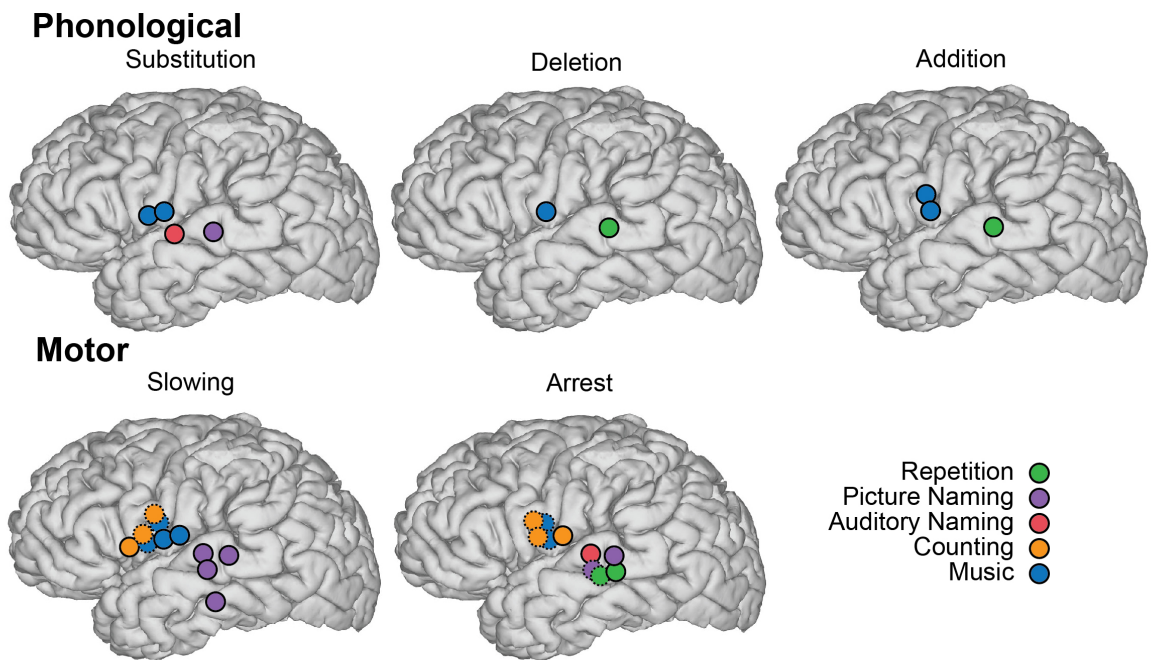


Figure 1: Stimulation-induced errors for speech and music tasks in Patient 1. Error types were divided into phonological (top row) and motor (bottom row), and different patterns of errors were observed across the five different tasks. Sites marked with dotted circles indicate overlap between tasks (markers were shifted for visibility). All sites shown had error rates that were above the 95% confidence interval of a shuffled distribution across all tested sites.

During repetition (16 sites tested), we observed two types of phonological errors (deletion and addition; **Fig. 1, green**). These errors were associated with stimulation to posterior STG, and involved the same site over the dorsal portion of the gyrus. Speech

arrest was also observed at two sites that were clustered in the posterior STG, and included the same site that induced phonological errors (**Fig. 2**).

During picture naming (13 sites tested), we observed one phonological error (substitution), which was induced by stimulation to a posterior STG site that was 4mm anterior to the sites that showed phonological errors during repetition (the same sites were stimulated in both tasks, but produced errors in only one task; **Fig. 1, purple**). Motor errors were observed with stimulation to posterior STG and inferior temporal gyrus (ITG). Slowing errors were observed when three sites on posterior STG and one site on ITG were stimulated, including the site that caused phonological errors during repetition. Finally, two of the same posterior STG sites that caused slowing errors during picture naming also caused speech arrest on other trials. One of these sites (the most posterior-dorsal site) overlapped with a speech arrest site during repetition (**Fig. 2**).

During auditory naming (4 sites tested), we observed a substitution error that was associated with stimulation to one site in the dorsal mid-STG (**Fig. 1, red**). We also observed speech arrest during stimulation at one posterior STG site that was near sites that caused arrest during repetition (one electrode in the pair was shared across tasks; **Fig. 2**).

Finally, during counting (9 sites tested), only supra-Sylvian sites were tested. We did not observe any phonological errors, however we found multiple sites that caused slowing and speech arrest. Stimulation to posterior inferior frontal gyrus (IFG), and more specifically the pars opercularis, caused slowing and speech arrest, as did stimulation to ventral pre-central gyrus.

We performed a parallel experiment to the speech tasks, where we stimulated a range of temporal and supra-Sylvian cortical sites while Patient 1 played the piano (10

sites tested; all music sites were tested in at least one of the speech tasks). We observed all 3 types of phonological errors, and both motor errors, however more instances of motor errors were observed during the task. One site over ventral pre-central gyrus caused substitutions, deletions, and additions (**Fig. 1, blue** and **Fig. 2**). There was also another site 4mm dorsal to the pre-central gyrus that caused addition errors, and a site on pars opercularis that caused substitution errors. The same ventral pre-central and pars opercularis sites were also associated with both types of motor errors. These sites also overlapped with slowing and arrest errors evoked in the same sites during counting (**Fig. 1 blue** and **orange**).

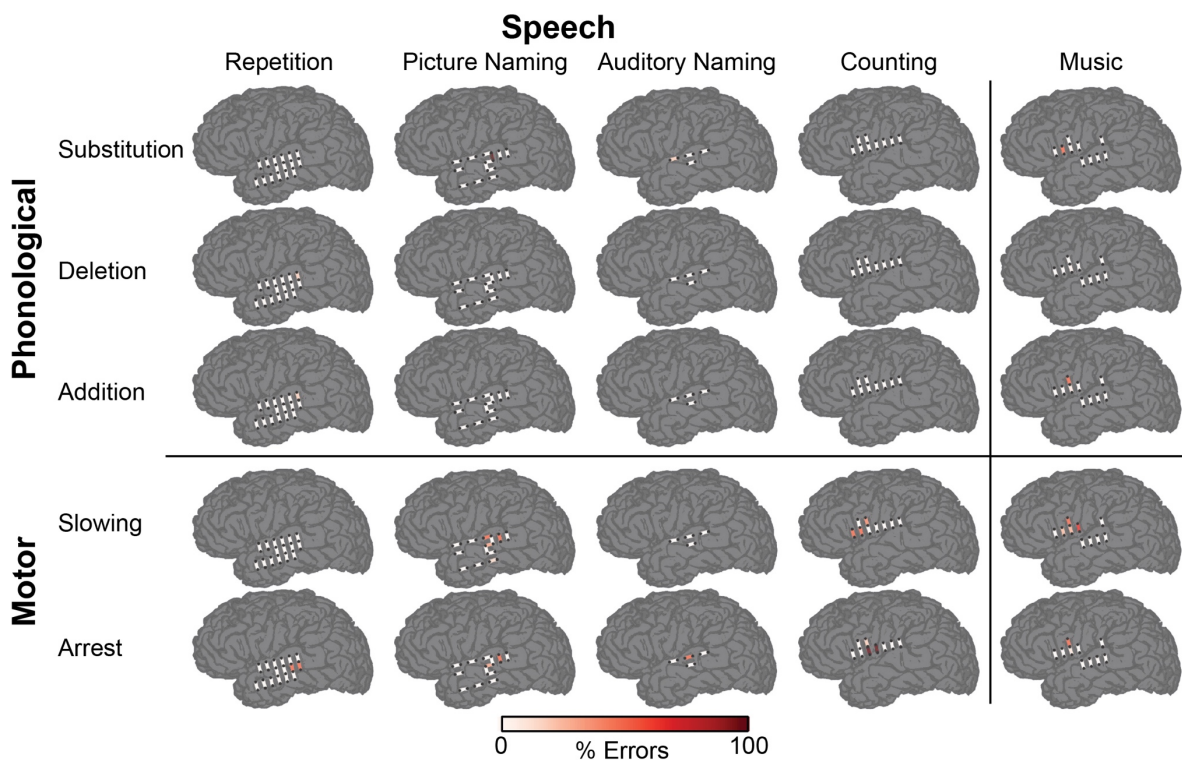


Figure 2: Percent errors across all error types and tasks for Patient 1. Only electrode pairs that were stimulated for a particular task are shown in each column.

We also examined whether there were differences between speech and music in terms of the latency between stimulation onset and error onset. Across all tasks, the

average stimulation-error latencies for music and speech tasks were 1.883 and 1.994 seconds, respectively ($t(32)=0.243$, $p=0.81$, two-tailed t-test with unequal variance). Given the limited number of errors for each task, we only further analyzed music vs. counting (both endogenously generated behaviors) for slowing and arrest (**Table 3**). For the purpose of this analysis, we treated arrest errors like “offset” errors, in which behaviour was arrested until after the offset of stimulation. We found a marginally significant effect where slowing errors occurred earlier in music than in counting ($p=0.0599$, Mann-Whitney U test). We also examined whether there was a difference in stimulation-error latencies for arrest, and found a marginally significant effect ($p=0.0571$, Mann-Whitney U test).

Table 3: Error latencies for Patient 1. Average (\pm standard deviation, where applicable) latencies between stimulation onset and error onset for each error type. Bold values indicate a significant difference in stimulation-error latency between counting and music.

	Speech				Music
	Repetition	Picture Naming	Auditory Naming	Counting	
Substitution	-- n=0	0.444 (n/a) n=1	2.856 (n/a) n=1	-- n=0	3.727 (n/a) n=2
Deletion	2.013 (n/a) n=1	-- n=0	-- n=0	-- n=0	1.182 (n/a) n=1
Addition	2.404 (n/a) n=1	-- n=0	-- n=0	-- n=0	4.005 (n/a) n=2
Slowing	2.935 (n/a) n=1	0.859 (1.219) n=4	-- n=0	2.959 (1.089) n=4	1.166 (0.552) n=9
Arrest	3.015 (n/a) n=2	0.435 (n/a) n=2	0.392 (n/a) n=1	1.846 (1.477) n=4	1.678 (0.821) n=3

Finally, Patient 2 underwent a similar mapping procedure during an awake surgery, where numerous sites throughout lateral frontal and parietal cortex were tested (**Fig. 3**). During the counting task, we identified sites on ventral pre-central gyrus (anterior bank), which were associated with speech errors. There were two sites in

particular where speech arrest was observed on 100% of trials during the first surgery. The same sites were stimulated while the patient strummed chords on a guitar, and we observed music arrest (i.e., complete immobility of the hands on the strings of the guitar) on 100% of trials (**Fig. 3**, red circle). Similar to Patient 1, stimulation at these same sites during rest did not evoke any movement or sensation. During Patient 2's second surgery, the more ventral site was observed to cause both counting and music arrest, however the exact number of trials for speech arrest during the counting task was not documented. Of note, across both surgeries, these were the only sites that were identified where speech and music arrest occurred, despite testing across lateral frontal and parietal sites (speech-specific errors were observed for repetition, picture naming, and counting in other regions; **Fig 3**). These results confirm, in an independent replication, the finding that stimulation of ventral pre-central gyrus results in both speech (vocal tract) and music (manual) errors.

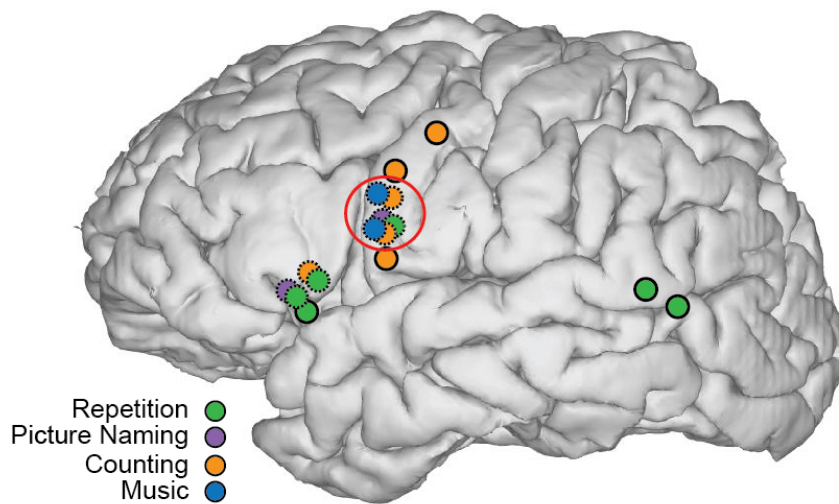


Figure 3: Stimulation-induced errors for speech and music tasks in Patient 2.

Errors were identified in the 3 speech tasks (repetition, picture naming, and counting) and for guitar playing (music). Sites marked with dotted circles indicate overlap between tasks (markers have been shifted for visibility). The red circle marks the locations of the two sites that showed stimulation-induced errors during the music task, also overlapping with speech errors.

4. Discussion

Here, we present two neurosurgical patients whose expert musical abilities allowed us to examine the extent to which the same cortical regions are necessary for speech and music production. We found that similar tasks involving highly practiced speech (counting) and musical sequences require left posterior IFG and ventral pre-central gyrus. In contrast, whereas many single word speech production tasks require

posterior STG auditory areas, stimulating those areas during music production do not disrupt behavior. These dissociations provide novel evidence for partially overlapping cortical networks involved in speech and music.

We found that posterior IFG (*pars opercularis*) is necessary for both speech (in particular, counting) and music production. In neurosurgery, this region is traditionally thought to be the localized site of Broca's area (Broca, 1861; Dronkers, Plaisant, Iba-Zizen, & Cabanis, 2007), as critical surgical decisions are often made to protect this site to prevent Broca's aphasia (Quiñones-Hinojosa, Ojemann, Sanai, Dillon, & Berger, 2003). Although this region is typically thought of as being involved in speech and language, recent evidence suggests that posterior IFG is not specific to speech, but may encode information about movement plans (Swann et al., 2009) and sequencing (Fadiga et al., 2009) in a domain-general manner. Despite its established role in speech, recent work has demonstrated that activity in Broca's area is correlated with linguistic and non-linguistic tasks (Koechlin & Jubault, 2006; Zatorre, Chen, & Penhune, 2007) including music (Koelsch et al., 2002; LaCroix et al., 2015; Maess et al., 2001), and even seems to serve similar functions in non-human primates (Wilson et al. 2015, 2017).

It is particularly striking that we observed disruption in music production for both piano and guitar, which involve different kinds of movements of the hands and arms, further suggesting a more domain-general mechanism. Furthermore, the fact that similar results were observed in a task (counting) that requires the control and movement of the vocal tract, but arguably does not involve the same core linguistic computations as other speech tasks, also suggests a non-linguistic function of this region. These findings of multiple functions attributed to left IFG may in fact reflect a more distributed mode of processing, in which this region plays dynamic and task-

dependent roles in concert with other areas that perform parallel computations (Duffau, 2017).

The present results add important information to this emerging picture. In particular, the fact that stimulation to inferior frontal regions causes arrest for both speech and music is consistent with their role in movement planning execution independent of the specific articulators used (Corina et al., 1999). Furthermore, these regions may be task-dependent, and involve the computation of abstract hierarchical structures necessary to carry out (and possibly understand (Leonard, Baud, Sjerps, & Chang, 2016)) complex sequential behaviors (Fadiga et al., 2009; Flinker et al., 2015; Pallier, Devauchelle, & Dehaene, 2011; Rao et al., 2017). The fact that we find both arrest and paraphasic errors in this region, depending on the task, supports the notion that both IFG and ventral pre-central gyrus have multiple functions at both the motor and cognitive levels.

The observation that stimulating the same sites in ventral pre-central gyrus disrupts speech and music production presents a striking and somewhat counterintuitive result. This region is typically associated with the laryngeal and vocal tract representations of the motor homunculus (Bouchard, Mesgarani, Johnson, & Chang, 2013; Penfield & Jasper, 1954). Here, we showed that stimulating this region disrupts both vocal tract and manual articulator movements. This raises the possibility that ventral pre-central regions are closely linked to neighboring pars opercularis, and may involve more complex representations that are independent of the articulators (Tate, Herbet, Moritz-Gasser, Tate, & Duffau, 2014).

Finally, a recent case report demonstrated that stimulating right STG caused errors in musical repetition for short phrases, but not for speech (Garcea et al., 2017). This raises the possibility that there is a complex relationship between task complexity

(sequences vs. single words or short phrases), hemisphere (left vs. right), and modality (speech vs. music) (LaCroix et al., 2015; Tate et al., 2014). The present results complement previous findings by demonstrating that whereas there may be speech-preferent representations in left superior temporal cortex (Leonard, Cai, et al., 2016), and music-specific representations in right superior temporal cortex (Garcea et al., 2017), inferior frontal cortex is necessary for both speech and music, perhaps especially when the task involves complex sequences.

There are several aspects of the present study that limit our ability to provide such interpretations unambiguously. First, since both patients were evaluated in neurosurgical contexts for pathological conditions, it is not possible to state whether the results will generalize to healthy populations (although they agree broadly with previous non-invasive neuroimaging and electrophysiological studies). Second, although we observed similarities between the two participants in the present study, their highly different pathologies (epilepsy and tumor) limit a direct comparison. In particular, since patient 1 had a chronic condition since childhood, it is possible that cortical reorganization had occurred. Furthermore, differences between bedside mapping (patient 1) and intraoperative mapping (patient 2) require different priorities due to time and safety constraints. Thus, although we observed broad agreement between the two patients in the present study, we are unable to fully account for the potential impacts of these differences. Further studies with these types of rare cases will help confirm the results presented here.

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Disclosure of interest

The authors report no conflicts of interest.

References

- Bouchard, K. E., Mesgarani, N., Johnson, K., & Chang, E. F. (2013). Functional organization of human sensorimotor cortex for speech articulation. *Nature*, *495*(7441), 327–332.
- Breshears, J. D., Molinaro, A. M., & Chang, E. F. (2015). A probabilistic map of the human ventral sensorimotor cortex using electrical stimulation. *Journal of Neurosurgery*, *123*(2), 340–349.
- Broca, P. (1861). Remarks on the seat of the faculty of articulated language, following an observation of aphemia (loss of speech). *Bulletin de La Société Anatomique*, *6*, 330–57.
- Chang, E. F., Breshears, J. D., Raygor, K. P., Lau, D., Molinaro, A. M., & Berger, M. S. (2017). Stereotactic probability and variability of speech arrest and anomia sites during stimulation mapping of the language dominant hemisphere. *Journal of Neurosurgery*, *126*(1), 114–121.

- Corina, D. P., McBurney, S. L., Dodrill, C., Hinshaw, K., Brinkley, J., & Ojemann, G. (1999). Functional roles of Broca's area and SMG: evidence from cortical stimulation mapping in a deaf signer. *Neuroimage*, *10*(5), 570–581.
- Dronkers, N. F., Plaisant, O., Iba-Zizen, M. T., & Cabanis, E. A. (2007). Paul Broca's historic cases: high resolution MR imaging of the brains of Leborgne and Lelong. *Brain*, *130*(5), 1432–1441.
- Duffau, H. (2017). The error of Broca: From the traditional localizationist concept to a connectomal anatomy of human brain. *Journal of Chemical Neuroanatomy*.
- ELAN. (2017). (Version Version 5.0.0-beta). Nijmegen: Max Planck Institute for Psycholinguistics. Retrieved from <https://tla.mpi.nl/tools/tla-tools/elan/>
- Fadiga, L., Craighero, L., & D'Ausilio, A. (2009). Broca's area in language, action, and music. *Annals of the New York Academy of Sciences*, *1169*(1), 448–458.
- Flinker, A., Korzeniewska, A., Shestyuk, A. Y., Franaszczuk, P. J., Dronkers, N. F., Knight, R. T., & Crone, N. E. (2015). Redefining the role of Broca's area in speech. *Proceedings of the National Academy of Sciences*, *112*(9), 2871–2875.
- Garcea, F. E., Chernoff, B. L., Diamond, B., Lewis, W., Sims, M. H., Tomlinson, S. B., ... Erickson, S. (2017). Direct Electrical Stimulation in the Human Brain Disrupts Melody Processing. *Current Biology*, *27*(17), 2684–2691.
- Hamilton, L. S., Chang, D., Lee, M., & Chang, E. F. (In Press). Semi-automated anatomical labeling and inter-subject warping of high-density intracranial recording electrodes in electrocorticography. *Frontiers in Neuroinformatics*. <https://doi.org/10.3389/fninf.2017.00062>
- Katlowitz, K. A., Oya, H., Howard, M. A., Greenlee, J. D., & Long, M. A. (2017). Paradoxical vocal changes in a trained singer by focally cooling the right superior temporal gyrus. *Cortex*, *89*, 111–119.

- Koechlin, E., & Jubault, T. (2006). Broca's area and the hierarchical organization of human behavior. *Neuron*, *50*(6), 963–974.
- Koelsch, S. (2011). Toward a neural basis of music perception—a review and updated model. *Frontiers in Psychology*, *2*.
- Koelsch, S., Gunter, T. C., Cramon, D. Y. v, Zysset, S., Lohmann, G., & Friederici, A. D. (2002). Bach speaks: a cortical “language-network” serves the processing of music. *Neuroimage*, *17*(2), 956–966.
- LaCroix, A. N., Diaz, A. F., & Rogalsky, C. (2015). The relationship between the neural computations for speech and music perception is context-dependent: an activation likelihood estimate study. *Frontiers in Psychology*, *6*.
- Leonard, M. K., Baud, M. O., Sjerps, M. J., & Chang, E. F. (2016). Perceptual restoration of masked speech in human cortex. *Nature Communications*, *7*, 13619.
- Leonard, M. K., Cai, R., Babiak, M. C., Ren, A., & Chang, E. F. (2016). The perisylvian cortical networks underlying single word repetition revealed by electrocortical stimulation and direct neural recordings. *Brain and Language*.
- Maess, B., Koelsch, S., Gunter, T. C., & Friederici, A. D. (2001). Musical syntax is processed in Broca's area: an MEG study. *Nature Neuroscience*, *4*(5), 540–545.
- Martin, S., Mikutta, C., Leonard, M. K., Hungate, D., Koelsch, S., Chang, E. F., ... Pasley, B. N. (2017). Neural Encoding of Auditory Features during Music Perception and Imagery: Insight into the Brain of a Piano Player. *bioRxiv*, 106617.
- Norman-Haignere, S., Kanwisher, N. G., & McDermott, J. H. (2015). Distinct Cortical Pathways for Music and Speech Revealed by Hypothesis-Free Voxel Decomposition. *Neuron*, *88*(6), 1281–1296.

- Özdemir, E., Norton, A., & Schlaug, G. (2006). Shared and distinct neural correlates of singing and speaking. *Neuroimage*, *33*(2), 628–635.
- Pallier, C., Devauchelle, A.-D., & Dehaene, S. (2011). Cortical representation of the constituent structure of sentences. *Proceedings of the National Academy of Sciences*, *108*(6), 2522–2527.
- Patel, A. D. (2010). *Music, language, and the brain*. Oxford University Press, USA.
- Penfield, W., & Jasper, H. (1954). *Epilepsy and the functional anatomy of the human brain*.
- Quiñones-Hinojosa, A., Ojemann, S. G., Sanai, N., Dillon, W. P., & Berger, M. S. (2003). Preoperative correlation of intraoperative cortical mapping with magnetic resonance imaging landmarks to predict localization of the Broca area. *Journal of Neurosurgery*, *99*(2), 311–318.
- Rao, V. R., Leonard, M. K., Kleen, J. K., Lucas, B. A., Mirro, E. A., & Chang, E. F. (2017). Chronic ambulatory electrocorticography from human speech cortex. *NeuroImage*, *153*, 273–282.
- Riva, M., Casarotti, A., Comi, A., Pessina, F., & Bello, L. (2016). Brain and music: an Intraoperative stimulation mapping study of a professional opera singer. *World Neurosurgery*, *93*, 486-e13.
- Swann, N., Tandon, N., Canolty, R., Ellmore, T. M., McEvoy, L. K., Dreyer, S., ... Aron, A. R. (2009). Intracranial EEG reveals a time-and frequency-specific role for the right inferior frontal gyrus and primary motor cortex in stopping initiated responses. *Journal of Neuroscience*, *29*(40), 12675–12685.
- Tate, M. C., Herbet, G., Moritz-Gasser, S., Tate, J. E., & Duffau, H. (2014). Probabilistic map of critical functional regions of the human cerebral cortex: Broca's area revisited. *Brain*, *137*(10), 2773–2782.

- Wilson, B., Kikuchi, Y., Sun, L., Hunter, D., Dick, F., Smith, K., ... Petkov, C. I. (2015). Auditory sequence processing reveals evolutionarily conserved regions of frontal cortex in macaques and humans. *Nature Communications*, 6.
- Wilson, B., Marslen-Wilson, W. D., & Petkov, C. I. (2017). Conserved sequence processing in primate frontal cortex. *Trends in Neurosciences*.
- Zatorre, R. J., Belin, P., & Penhune, V. B. (2002). Structure and function of auditory cortex: music and speech. *Trends in Cognitive Sciences*, 6(1), 37–46.
- Zatorre, R. J., Chen, J. L., & Penhune, V. B. (2007). When the brain plays music: auditory-motor interactions in music perception and production. *Nature Reviews. Neuroscience*, 8(7), 547.

Table 1: Error categories, coding criteria, and examples.

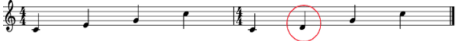


Error Category	Error Sub-type	Criteria	Example
Phonological	Substitution	Correct number of phonemes/notes, but production of an incorrect phoneme/note	<p>ɪntərdʒɛkʃən/ -> ɛntərdʒɛkʃən</p> 
	Deletion	Missing phoneme/note	<p>dɛləkəsi/ -> /ɛləkəsi</p> 
	Addition	Extra phoneme/note	<p>Broken Window → brok um broken.... wɪndəʊ</p> 
Motor	Slowing	Phonologically/musically correct, but produced at a slower pace	<p>“Prosperity” -> “pro---sper---ity”</p>
	Arrest	Complete halting of production	[no production during stimulation]

Table 2: Summary of stimulation across anatomical regions in Patient 1. Data are collapsed across tasks and regions were defined by the Freesurfer anatomical atlas. “M” refers to errors on the music task, and “S” refers to errors on the speech tasks.

	Temporal			Frontal			Parietal
	<i>STG</i>	<i>MTG</i>	<i>ITG</i>	<i>IFG</i>	<i>Pre-central</i>	<i>Post-central</i>	<i>SMG</i>
Substitution	n=2 3.4% (M: 0) (S: 2)	n=0 --	n=0 --	n=2 15.4% (M: 2) (S: 0)	n=1 2.9% (M: 1) (S: 0)	n=0 --	n=0 --
Deletion	n=1 1.7% (M: 0) (S: 1)	n=0 --	n=0 --	n=0 --	n=1 2.9% (M: 1) (S: 0)	n=0 --	n=0 --
Addition	n=1 1.7% (M: 0) (S: 1)	n=0 --	n=0 --	n=0 --	n=3 8.6% (M: 3) (S: 0)	n=0 --	n=0 --
Slowing	n=4 6.8% (M: 0) (S: 4)	n=0 --	n=1 100% (M: 0) (S: 1)	n=3 23.1% (M: 1) (S: 2)	n=10 28.6% (M: 8) (S: 2)	n=0 --	n=0 --
Arrest	n=5 8.5% (M: 0) (S: 5)	n=0 --	n=0 --	n=0 --	n=7 20.0% (M: 3) (S: 4)	n=0 --	n=0 --
Total Errors	13 (M: 0)	0 (M: 0)	1 (M: 0)	5 (M: 3)	22 (M: 16)	0	0

	(S: 13)	(S: 0)	(S: 1)	(S: 2)	(S: 6)		
Total Trials	59	16	1	13	35	7	4

Table 3: Error latencies for Patient 1. Average (\pm standard deviation, where applicable) latencies between stimulation onset and error onset for each error type. Bold values indicate a significant difference in stimulation-error latency between counting and music.

	Speech				Music
	Repetition	Picture Naming	Auditory Naming	Counting	
Substitution	-- n=0	0.444 (n/a) n=1	2.856 (n/a) n=1	-- n=0	3.727 (n/a) n=2
Deletion	2.013 (n/a) n=1	-- n=0	-- n=0	-- n=0	1.182 (n/a) n=1
Addition	2.404 (n/a) n=1	-- n=0	-- n=0	-- n=0	4.005 (n/a) n=2
Slowing	2.935 (n/a) n=1	0.859 (1.219) n=4	-- n=0	2.959 (1.089) n=4	1.166 (0.552) n=9
Arrest	3.015 (n/a) n=2	0.435 (n/a) n=2	0.392 (n/a) n=1	1.846 (1.477) n=4	1.678 (0.821) n=3

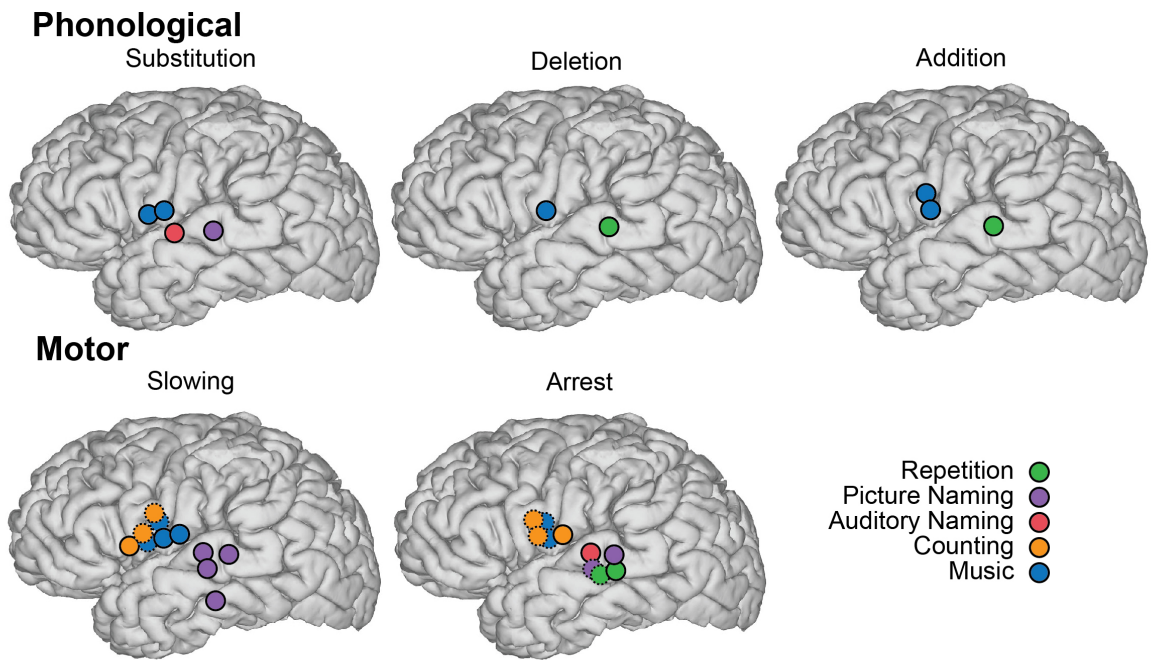


Figure 1: Stimulation-induced errors for speech and music tasks in Patient 1. Error types were divided into phonological (top row) and motor (bottom row), and different patterns of errors were observed across the five different tasks. Sites marked with dotted circles indicate overlap between tasks (markers were shifted for visibility). All sites shown had error rates that were above the 95% confidence interval of a shuffled distribution across all tested sites.

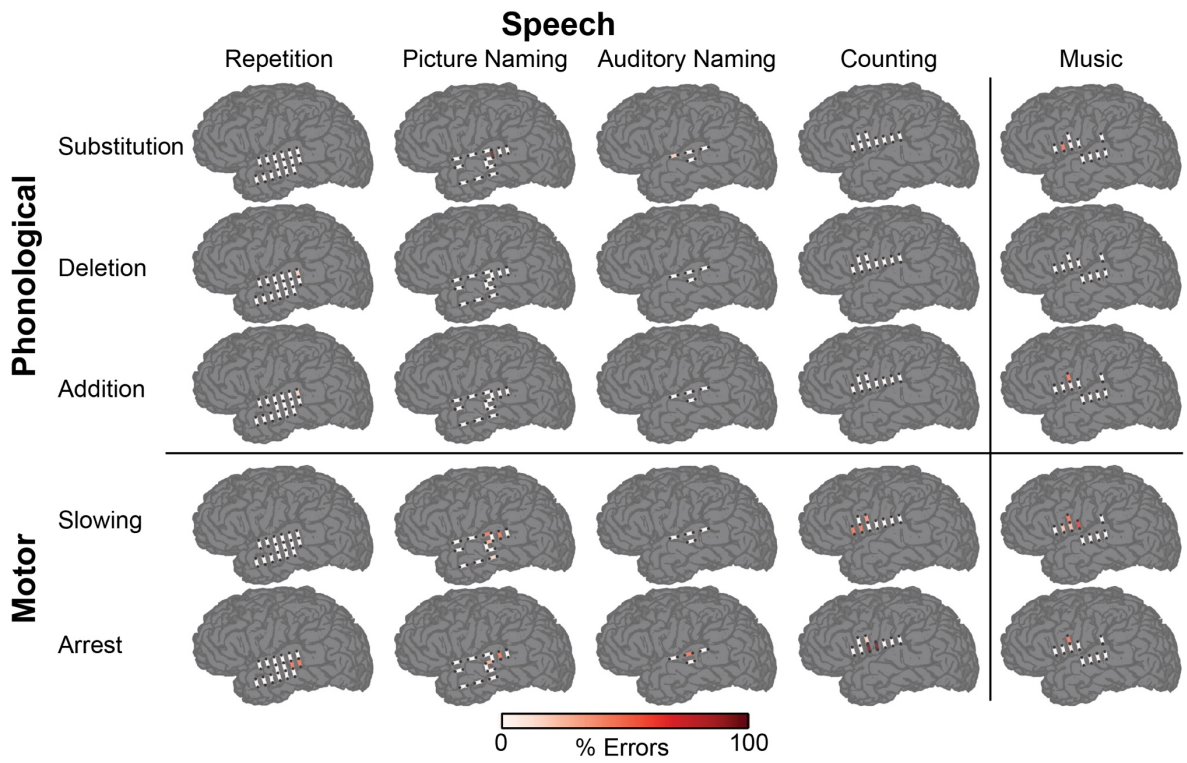


Figure 2: Percent errors across all error types and tasks for Patient 1. Only electrode pairs that were stimulated for a particular task are shown in each column.

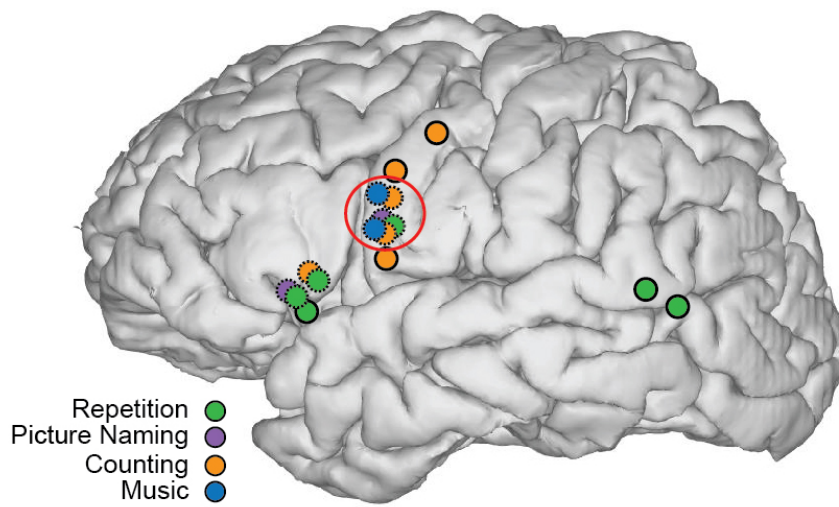


Figure 3: Stimulation-induced errors for speech and music tasks in Patient 2.

Errors were identified in the 3 speech tasks (repetition, picture naming, and counting) and for guitar playing (music). Sites marked with dotted circles indicate overlap between tasks (markers have been shifted for visibility). The red circle marks the locations of the two sites that showed stimulation-induced errors during the music task, also overlapping with speech errors.