Received: 10 November 2018 | Revised: 1 April 2019 | Accepted: 2 April 2019
DOI: 10.1002/hbm.24597

RESEARCH ARTICLE

WILEY

# Dissociating semantic and phonological contributions of the left inferior frontal gyrus to language production

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**Funding information**
German Research Foundation, Grant/Award Numbers: HA 6314/3-1, HA 6314/4-1, KL 2933/3-1; Max Planck Society

## Abstract

While the involvement of the left inferior frontal gyrus (IFG) in language production is undisputed, the role of specific subregions at different representational levels remains unclear. Some studies suggest a division of anterior and posterior regions for semantic and phonological processing, respectively. Crucially, evidence thus far only comes from correlative neuroimaging studies, but the functional relevance of the involvement of these subregions during a given task remains elusive. We applied repetitive transcranial magnetic stimulation (rTMS) over anterior and posterior IFG (aIFG/pIFG), and vertex as a control site, while participants performed a category member and a rhyme generation task. We found a functional-anatomical double dissociation between tasks and subregions. Naming latencies were significantly delayed in the semantic task when rTMS was applied to aIFG (relative to pIFG and vertex). In contrast, we observed a facilitation of naming latencies in the phonological task when rTMS was applied to pIFG (relative to aIFG and vertex). The results provide first causal evidence for the notion that anterior portions of the IFG are selectively recruited for semantic processing while posterior regions are functionally specific for phonological processing during word production. These findings shed light on the functional parcellation of the left IFG in language production.

KEYWORDS
Broca, prefrontal cortex, repetitive transcranial magnetic stimulation, virtual lesion, word generation

## 1 | INTRODUCTION

Since Paul Broca's famous patient “Monsieur Tan,” it is assumed that the left inferior frontal gyrus (IFG) is indispensable for intact language production in most humans. Specifically, research has shown that Brodmann areas (BA) 45 and 44, corresponding to anterior and posterior portions of the left IFG, respectively, are critically involved in language production (de Zubicaray & Piai, 2019). However, to what extent these regions are *selectively* recruited during different stages of language production remains unclear.

A meta-analysis of predominantly language comprehension studies has pointed toward an anterior–posterior division of labor of semantic and phonological processing, respectively (Vigneau et al., 2006). Likewise, an antero-posterior division of labor in the left IFG was suggested in the production domain during semantic and phonological verbal fluency tasks, respectively (Costafreda et al., 2006). However, this dissociation appears to be less stable across studies since a later meta-analysis found that BA 44 was preferentially activated during phonological fluency tasks, whereas both BA 44 and 45 were involved during semantic fluency tasks (Wagner, Sebastian, Lieb, Tüscher, & Tadić, 2014). In a previous study reporting analogous results, Heim, Eickhoff, and Amunts (2008) speculated that BA 45 underlies word retrieval in both tasks, whereas BA 44 is involved in the processing of the phonemic cue and syllabification. However, Klein et al. (1997) reported a case of a tumor patient who was unable to produce synonyms and name pictures, but whose word repetition skills remained unaffected when the left aIFG was stimulated intraoperatively. This suggests a selective role of the left aIFG for semantic, but not phonological processing during language production. Moreover, Katzev, Tüscher, Hennig, Weiller, and Kaller (2013) found that the anterior-dorsal parts of BA 45 are activated in a semantic fluency task when task difficulty is high enough.

Critically, exclusively examining the BOLD response during a given task and comparing it between tasks may not be sufficient to unveil functional specializations of a given brain region. Directly interfering with the neuronal activity of a circumscribed region, as is done with transcranial magnetic stimulation (TMS), may be a more direct way to test a potential parcellation. For language comprehension tasks, some TMS studies showed task-specific interference in response to aIFG or pIFG stimulation. Devlin, Matthews, and Rushworth (2003) reported longer reaction times in a conceptually driven task (is an object man-made or natural?, i.e., semantic), but not during a syllable judgment task (does a word have two or three syllables?, i.e., phonological) during aIFG stimulation. In a similar task setup, we found longer reaction times in a phonological task during pIFG relative to aIFG stimulation, but no selective performance decrement in a semantic task (Hartwigsen et al., 2010). Most similar to the current study, Gough, Nobre, and Devlin (2005) found a double dissociation of aIFG and pIFG for semantic and phonological word processing (synonym and homophone judgment, respectively).

However, it remains unclear whether the reported functional-anatomical double dissociation also holds for language production. TMS over the left IFG has been used to induce speech arrest (Epstein et al., 1996, 1999; Pascual-Leone, Gates, & Dhuna, 1991) and language disruption (Rogić, Deletis, & Fernández-Conejero, 2014) during production tasks like picture naming and counting, revealing a causal role of this region in the overt production of both spontaneous and overlearned utterances. Chouinard, Whitwell, and Goodale (2009) reported longer naming latencies during pIFG stimulation in an object naming, color naming, and categorization task. Furthermore, a number of studies adopted a chronometric approach and showed an increase of picture naming latencies when the pulse was applied to a posterior portion of the IFG between 225 and 375 ms after picture onset (Schuhmann, Schiller, Goebel, & Sack, 2009; Shinshi et al., 2015; Wheat et al., 2013; Zhang, Yu, Zhang, Jin, & Li, 2018), arguing for a role of this region in syllabification (Indefrey, 2011). However, these studies were not able to make specific distinctions between different processing levels throughout the production process, as they only employed simple picture naming tasks in which semantic and phonological contributions cannot be disentangled. Moreover, all of these studies selectively targeted one area of the IFG, which does not speak to a potential parcellation of this rather big cortical area.

The aim of the current study was to test the behavioral specificity of the anterior and posterior IFG during semantic and phonological processing in language production. By applying short bursts of repetitive transcranial magnetic stimulation (rTMS) to either one of these regions while participants performed a semantic and a phonological production task, we measured how transient disruption of either node affected behavior on the semantic and the phonological level. If the aIFG is a key node for semantic aspects of language production, we expected longer naming latencies and/or more errors during the semantic production task (category member generation) when this area was perturbed with rTMS. Conversely, if the pIFG is crucial for phonological aspects of language production, we expected longer naming latencies and/or more errors during the phonological production task (rhyme generation) when this area was targeted. To test for functional-anatomical specificity, we compared perturbation of either area with rTMS of the respective other region and stimulation of a control site in the vertex during each task. If neither of these areas are sensitive to one or the other processing level, no differences should be found between tasks and stimulation sites.

## 2 | MATERIALS AND METHODS

The study design and analysis plan were preregistered at the Open Science Framework (OSF; https://osf.io/vqynu/). Raw, coded data, and analysis scripts can be found at https://osf.io/u64e5/.

### 2.1 | Participants

Twenty-four native speakers of German (12 females, mean age: 27.3 years, *SD* = 3.9, range = 20–34) with no history of neurological disorders or TMS contraindications participated in our study. They were recruited via the participant database at the Max Planck Institute for Human Cognitive and Brain Sciences and individually invited via phone calls. All participants were right-handed (mean handedness score = 90.2, *SD* = 9.2, range = 71–100). All had obtained the Abitur (German equivalent of high-school diploma) and 21 out of 24 participants had completed or were still pursuing an academic education, suggesting an overall comparable educational level. One participant was replaced due to an overall mean error rate of 41.8%. Written informed consent was obtained before the experiment. The study was performed according to the guidelines of the Declaration of Helsinki and approved by the local ethics committee at the Medical Faculty of the University of Leipzig (118/16-eK).

### 2.2 | Experimental design and procedures

We used a 2 × 3 factorial within-subject design including the factors *task* (phonological vs. semantic) and *stimulation site* (aIFG vs. pIFG vs. vertex). In three sessions that were at least 6 days apart to prevent carry-over effects, we applied TMS to the left aIFG, pIFG, or vertex while participants performed both production tasks (see Figure 1a). Tasks were blocked, and participants were always given the same task order throughout the experimental sessions (i.e., semantic task first or phonological task first). The order of stimulation sites and tasks was counterbalanced across participants. Responses were recorded for offline analysis via a microphone (Røde NT55) placed next to the participant and connected to the experimenter computer. Stimulus presentation and utterance recording was controlled using the software Presentation (Neurobehavioral Systems, Inc., Berkeley, CA; www.neurobs.com).

### 2.3 | Tasks

All participants performed a semantic and a phonological production task (see Figure 1b). In the semantic task, participants were asked to produce a

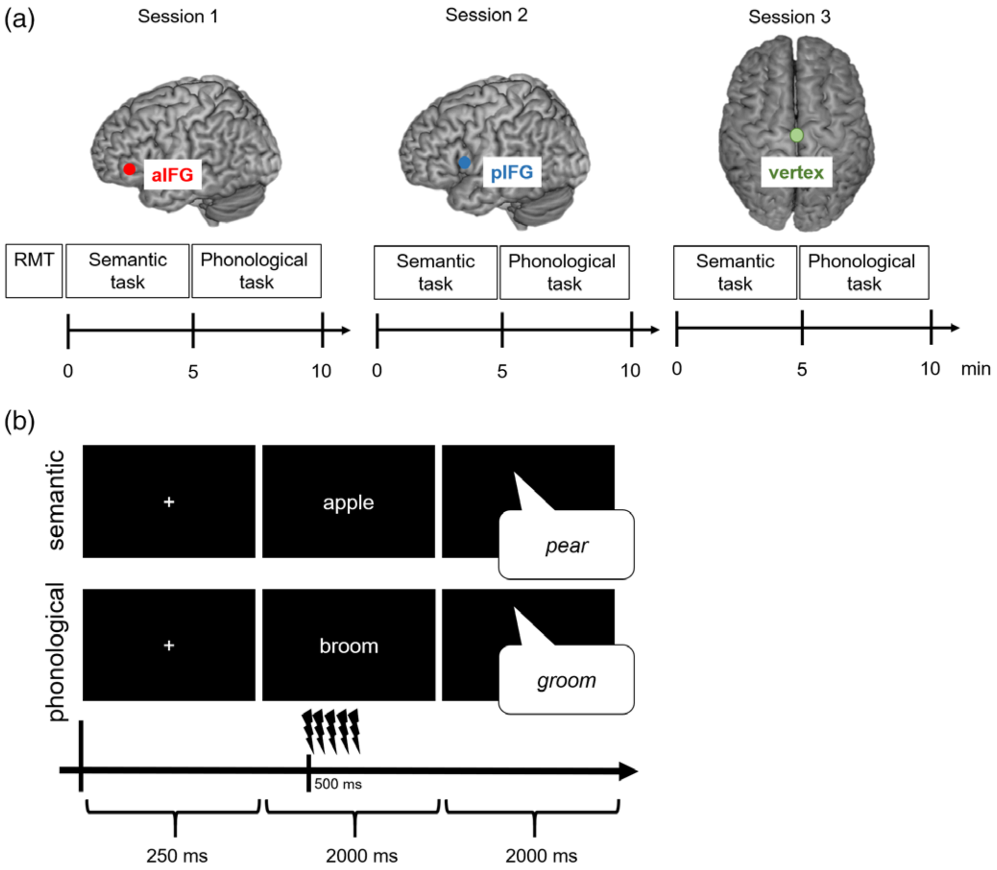


**FIGURE 1** Experimental design and task outline. (a) during the first session, individual RMT was determined. Throughout the three experimental sessions, participants received rTMS either over the left aIFG (MNI coordinates: $x, y, z = -52, 34, -6$), left pIFG (MNI coordinates: $x, y, z = -52, 16, 8$ mm), or vertex, respectively, while performing the semantic and the phonological task. The order of sessions and tasks was counterbalanced across participants. (b) Illustration of a trial for the semantic and phonological task, respectively. Five pulses of TMS were applied at a frequency of 10 Hz 500 ms after stimulus onset during each trial [Color figure can be viewed at wileyonlinelibrary.com]

member of the same category as the word presented on the screen (e.g., upon seeing "Apfel" [apple], they would have to produce another fruit). In the phonological task, participants were asked to produce a word, preferably a noun, that rhymed with the word presented on the screen (e.g., upon seeing "Besen" [broom], they would have to produce for instance "Wesen" [being], or "Tresen" [counter]). Participants were instructed to respond as quickly and accurately as possible as soon as the word appeared on the screen. Each task had a duration of ~5 min.

Three hundred and eighteen mono- and disyllabic German nouns matched for frequency (based on SUBTLEX-DE norms, Brysbaert et al., 2011) and length (*ps* > 0.126) were taken from a behavioral pilot study with 16 participants who did not take part in the main study. Items were included in the study if at least half of the participants in the pilot study were able to produce a correct response. All items (159 per task) were split in three experimental lists, the order of which was counterbalanced across participants and stimulation site to the best degree possible. Three additional items per task were selected for use in warm-up and practice trials.

## 2.4 | Repetitive rTMS

We used neuronavigated rTMS (TMS Navigator, Localite, Sankt Augustin, Germany) based on co-registered individual T1-weighted MRI images to navigate the TMS coil and maintain its exact location and orientation throughout all sessions. T1-weighted images were taken from the in-house database and had previously been obtained at a 3-Tesla Siemens scanner (Siemens Healthcare, Erlangen, Germany) using a magnetization-prepared rapid gradient echo (MPRAGE) sequence in sagittal orientation (inversion time = 650 ms, repetition time = 300 ms, flip angle = 10°, field of view = 256 mm × 240 mm, voxel-size = 1 mm × 1 mm × 1.5 mm).

TMS was applied using the mean Montreal Neurological Institute (MNI) coordinates for the left aIFG ($x, y, z = -52, 34, -6$) and pIFG ($x, y, z = -52, 16, 8$ mm) described in Gough et al. (2005). Based on these coordinates, the individual stimulation sites were determined by calculating the inverse of the normalization transformation and transforming these coordinates from standard to individual space for each subject using SPM 8 (Welcome Trust Center for Neuroimaging, University College London, UK) in Matlab 9.3 (The Mathworks, Inc.). The vertex was determined manually as the midpoint between the lines connecting nasion and inion and tragi of the left and right ear.

The coil was placed tangentially on the head with the handle pointing at 45° to the sagittal plane and the second phase of the biphasic pulse inducing a posterior to anterior current flow. Stimulation intensity was set to 90% of individual resting motor threshold (RMT) as in our previous TMS studies on language comprehension (Hartwigsen et al., 2010; Kuhnke, Meyer, Friederici, & Hartwigsen, 2017). RMT was measured at the beginning of the first session, and the same value was used for all three experimental sessions as in our previous TMS studies (Kuhnke et al., 2017; Meyer, Elsner, Turker, Kuhnke, & Hartwigsen, 2018) to guarantee that the TMS intensity was similar for all TMS sessions and sites within each participant. RMT was defined as the lowest stimulus intensity producing at least five visible motor evoked potentials in the relaxed first dorsal interosseus muscle of the right hand when stimulating the hand region of the primary motor cortex ten times. Mean stimulation intensities were 37.3 ± 7.0%, 37.5 ± 7.5%, and 39.1 ± 7.0% of total stimulator output for aIFG, pIFG, and vertex, respectively. A figure-of-eight-shaped coil (double 60 mm; coil type CB-60) connected to a MagPro X100 stimulator (MagVenture, Farum, Denmark) was used in all TMS conditions. During each experimental trial, a five-pulse train of stereotactically guided 10 Hz TMS was applied over left aIFG, left pIFG, or vertex 500 ms after stimulus onset, resulting in a stimulation window extending up until 1,000 ms after stimulus onset. We chose this stimulation window to avoid that TMS merely affected the processing of the visual stimulus (i.e., the word). Instead, by applying the pulses at a later time point, we ensured that their effect unfolded throughout the neurocognitive operations associated with lexical access in production, as opposed to mere comprehension of the word. Evidence from electrophysiological studies suggests that processing a printed word is completed at around 400–500 ms after stimulus onset (Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999; Pylkkänen & Marantz, 2003). We therefore decided to apply stimulation after this initial word processing stage in order to be closer to the processing stages of production. Timing of the stimulation was controlled via Presentation software.

## 2.5 | Data analysis

Naming latencies and error rates were analyzed separately, with the former selectively including correct responses. Naming latencies deviating from a participant's mean (aggregated by task and stimulation site) by more than three *SD*s were treated as outliers and removed from the analysis (59 observations, 0.8% of all trials). The remaining responses were coded offline for accuracy. Missing, erroneous, and repaired responses (e.g., “br-broom” or “t … err … pear”) were subjected to error rate analyses (1,156 observations, 15.1% of all trials). Additionally, eight observations (0.1% of all trials) were removed because the software failed to record the vocal response. Naming latencies of correct responses were measured manually to the closest millisecond using Praat software (Boersma & Weenink, 2018).

Naming latencies and error rates were analyzed with generalized linear mixed effects models (GLMEMs) using the lme4 package (version 1.1-13; Bates, Mächler, Bolker, & Walker, 2015) in R (version 3.4.1; www.r-project.org). Contrary to linear mixed effects models, GLMEMs account for the right-skewed shape of the naming latency distribution, rendering a transformation of the raw data obsolete (Lo & Andrews, 2015). For the naming latency data, we fitted an identity function, which presumes that the naming latencies directly tap the underlying cognitive process (i.e., semantic and phonological processing in language production, respectively) of interest, to a Gamma distribution (i.e., right-skewed with a long tail in the slow responses). Error rates were analyzed using mixed logit regression, which, unlike classical analyses of variance, are able to accommodate the binomial distribution of binary responses (Jaeger, 2008). All analyses included the fixed effects task (semantic vs. phonological) and stimulation site (aIFG vs. pIFG vs. vertex) as well as random effects for participants and items, with participant random slopes for stimulation site and task. For the three-level fixed effect stimulation site, we set the vertex as the reference level, since this site represented the control site.

## 3 | RESULTS

### 3.1 | rTMS reveals a functional-anatomical double dissociation in the left IFG

Table 1 displays naming latencies and error rates broken down by task and stimulation site, and all results for the inferential statistics can be found in the Supporting Information.

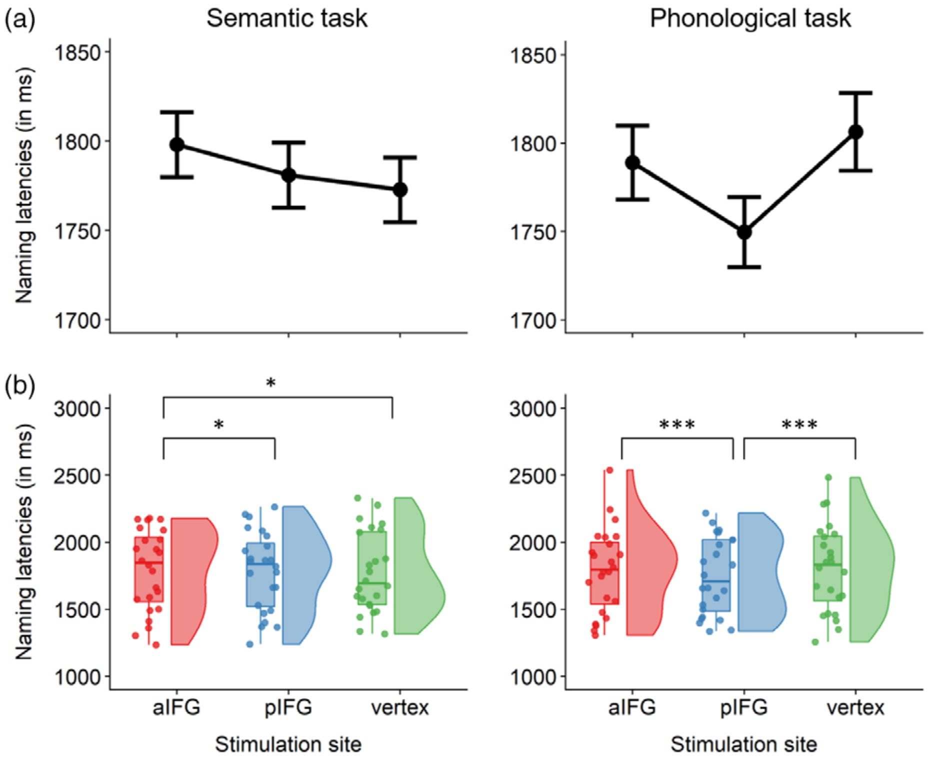
Naming latencies did not differ between tasks ($p > .092$). Relative to rTMS over the vertex, rTMS over the aIFG increased naming latencies ($\beta = 18.93$, $SE = 3.97$, $z = 4.8$, $p < .001$), whereas rTMS over the pIFG decreased naming latencies ($\beta = -15.88$, $SE = 5.56$, $z = -2.9$, $p = .004$). Importantly, there was an interaction between task and stimulation, both when comparing vertex relative to aIFG ($\beta = -17.27$, $SE = 5.50$, $z = -3.1$, $p = .002$) and pIFG ($\beta = -30.39$, $SE = 3.73$, $z = -8.1$, $p < .0001$). We thus analyzed the simple effects of rTMS separately for both tasks.

For the semantic task, naming latencies increased in response to rTMS over the aIFG ($\beta = 19.15$, $SE = 8.96$, $z = 2.1$, $p = .033$), but not in response to rTMS over the pIFG ($p > .808$). To ensure that rTMS over the aIFG resulted in a selective increase of naming latencies both compared to vertex and pIFG stimulation, we ran an additional analysis in which we set the aIFG as reference level. This analysis confirmed that under aIFG stimulation, naming latencies significantly increased compared to pIFG stimulation ($\beta = -20.90$, $SE = 6.32$, $z = -3.3$, $p < .001$) and vertex stimulation ($\beta = -19.15$, $SE = 6.75$, $z = -2.8$, $p = .005$; Figure 2, left panels).

**TABLE 1** Means, mean standard errors, and 95% confidence intervals for naming latencies (response times, [RT] in ms) and error rates (ER, in %), broken down by task (semantic vs. phonological) and stimulation site (aIFG vs. pIFG vs. vertex)

| | Semantic task | | | | | | Phonological task | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | RT | | | ER | | | RT | | | ER | | |
| | *M* | *SE* | CI 95% | *M* | *SE* | CI 95% | *M* | *SE* | CI 95% | *M* | *SE* | CI 95% |
| aIFG | 1,798 | 18 | 1,762–1,834 | 10.6 | 0.9 | 10.4–10.8 | 1,789 | 21 | 1,748–1,830 | 19.4 | 1.1 | 19.2–19.6 |
| pIFG | 1,781 | 18 | 1,745–1,817 | 10.8 | 0.9 | 10.6–11.0 | 1,750 | 20 | 1,711–1,789 | 19.2 | 1.1 | 19.0–19.4 |
| Vertex | 1,773 | 18 | 1,737–1,809 | 11.6 | 0.9 | 11.4–11.8 | 1,807 | 22 | 1,764–1,850 | 19.2 | 1.1 | 19.0–19.4 |

**FIGURE 2** Illustration of the results of the naming latency analysis, broken down by task and stimulation site. (a) raw naming latencies (± *SEM*). (b) raincloud plots (Allen, Poggiali, Whitaker, Marshall, & Kievit, 2018) of naming latencies aggregated by participants. *$p < .05$; ***$p < .001$ [Color figure can be viewed at wileyonlinelibrary.com]



By contrast, for the phonological task, naming latencies significantly decreased in response to rTMS over the pIFG ($\beta = -64.03$, $SE = 7.10$, $z = -9.0$, $p < .0001$), but not in response to rTMS over the aIFG ($p > .184$). We likewise ran an additional analysis in which we set the pIFG as the reference level. This confirmed that naming latencies were selectively facilitated under pIFG stimulation compared to aIFG stimulation ($\beta = 54.63$, $SE = 6.51$, $z = 8.4$, $p < .0001$) and vertex stimulation ($\beta = 64.03$, $SE = 7.22$, $z = 8.9$, $p < .0001$; Figure 2, right panels).

For the analysis of error rates, there was a significant main effect of task ($\beta = 0.40$, $SE = 0.09$, $z = 4.1$, $p < .0001$), implying higher error rates for the phonological compared to the semantic task. None of the other effects were significant (*ps* > .585).

### 3.2 | Additional analyses

Due to the three-session nature of the current study and the associated possibility of a confounding influence of practice effects, we ran an additional analysis in which we added the by-participant slope of session (first, second, or third) to the random-effects structure. However, the result pattern remained unchanged (see Tables S3 and S4), suggesting that the overall results were not contaminated by potential practice effects built up by the repetition of the tasks across sessions.

In 3.1% of the correct trials (195 data points), participants responded before the last pulse of the rTMS train had subsided (i.e., faster than 1,000 ms). To ensure that these responses, which may have interfered with the overt motor response of speaking, did not obscure the effects reported above, we ran an additional analysis in which we excluded all responses faster than 1,000 ms. However, this did not change the overall pattern: rTMS over the left aIFG still selectively slowed naming responses in the semantic task, whereas rTMS over the left pIFG still selectively sped up naming responses in the phonological task. The results from this additional analysis can be found in Table S5.

## 4 | DISCUSSION

The goal of the current study was to investigate the functional specificity of anterior and posterior regions of the left IFG during language production tasks that selectively required semantic and phonological processing, respectively. In a language production experiment with concurrent rTMS, we found a functional-anatomical double dissociation: Stimulating the left aIFG selectively increased naming latencies in the semantic task, whereas stimulating the left pIFG selectively decreased naming latencies in the phonological task, relative to the other two stimulation sites. Our data provide causal evidence for a locally specific division of labor for semantic and phonological contents within the left IFG which holds not only for language comprehension––as has been shown in previous studies (e.g., Gough et al., 2005; Vigneau et al., 2006)––but also for language production. These results are in good agreement with a previous meta-analysis on neuroimaging data that also suggested an antero-posterior division of labor in the left IFG during semantic and phonological verbal fluency tasks, respectively (Costafreda et al., 2006).

However, these findings appear to be in discordance with previous fMRI studies that reported a selective involvement of BA 44 in a phonological fluency task, but comparable activation in BA 45 in a semantic and phonological fluency task (Heim et al., 2008; Heim, Eickhoff, & Amunts, 2009), leading to the assumption that only the posterior regions of the left IFG exert a function that is tuned to a specific representational level during language production. Our results are in contrast to this because we also find a selective involvement of the aIFG in a semantic production task. However, it needs to be noted that the area we stimulated, which was derived from a previous rTMS study on word comprehension (Gough et al., 2005), was located in the anterior-ventral part of BA 45 and BA 47 (i.e., anterior to the portion of BA 45 investigated by Heim and colleagues; see Figure 1a), which has also been implicated in semantic processing in previous neuroimaging studies (Binder, Desai, Graves, & Conant, 2009; Devlin et al., 2003; Fiez, 1997; Katzev et al., 2013; Vigneau et al., 2006). It is thus possible that Heim et al. (2008, 2009) found no selective activation for semantic production because their regions of interest did not include the anterior part targeted in our study (see also Hartwigsen et al., 2010). Although they do report that no specific activation was found in BA 47 in a whole-brain analysis, this effect may have been too weak to be detectable following multiple comparisons. We propose that the posterior-dorsal portion of BA 45 adjacent to BA 44 may potentially constitute a "convergence zone" between semantic and phonological processing, which would also be in line with the conclusions drawn by Heim et al. (2009). Future studies could thus test whether there is a gradient of specificity within left BA 45, with the anterior-ventral part bordering BA 47 being more specialized and the posterior-dorsal part being less specialized for semantic processing. However, due to the limited spatial resolution of most conventional TMS coils that lies in the range of approximately 2 cm (Sandrini, Umiltà, & Rusconi, 2011), this question might be best tackled with either highly focal mini coils (e.g., Groppa et al., 2012), electrocorticography, or high-resolution neuroimaging.

Furthermore, Heim et al. (2008) may have failed to find functionally specific activation in the semantic fluency task because their task did not require sufficient cognitive resources, as task difficulty has been shown to be sensitive to different anterior regions during semantic processing. Katzev et al. (2013) reported that an area overlapping with the aIFG as stimulated in our study on the anterior–posterior axis (MNI coordinates: $x = -53$, $y = 33$, $z = 18$) was engaged when processing demands were high (i.e., when word retrieval was more difficult) in a semantic fluency task. In an additional exploratory analysis of our dataset, we could confirm this finding: When removing items which likely elicited a more automated response (e.g., with antonyms like "salt–pepper", "man–woman") from the stimulus set, responses during aIFG stimulation were, on average, 45 ms slower ($M$ = 1,877 ms, $SE$ = 20) than responses during vertex stimulation ($M$ = 1,832 ms, $SE$ = 20, $p < .001$) and 26 ms slower than during pIFG stimulation ($M$ = 1,851 ms, $SE$ = 20, $p < .001$). In other words, the anterior subregion targeted in our study may be involved in more effortful semantic processing in which a lexical candidate needs to be selected from a variety of choices, whereas highly frequent, more automatic responses rely less on this region. Notably, a key role of the left aIFG in executively demanding semantic tasks was also demonstrated in previous TMS studies on word comprehension, arguing for a specific contribution of this region to the controlled retrieval and selection of semantic knowledge (Whitney, Kirk, O'Sullivan, Lambon Ralph, & Jefferies, 2011, 2012). In one of these previous studies (Whitney et al., 2011), rTMS of the aIFG selectively disrupted executively demanding semantic judgments while leaving semantic decisions based on strong automatic associations unaffected. Together, the previous and present study suggest that the left aIFG might play a key role in the processing of executively demanding semantic tasks, in both language comprehension and production. Future studies could aim to disentangle this dissociation in production by orthogonally manipulating the amount of competition elicited with different item sets.

Contrary to our hypothesis, pIFG stimulation facilitated responses in the phonological task relative to rTMS over the aIFG and the vertex. Based on the study by Gough et al. (2005), we had expected that in the event of a functional involvement of the pIFG in phonological processing during language production, rTMS over this region should *increase* naming latencies compared to aIFG and vertex. Yet, the effects of TMS on neural activity might also give rise to a "paradoxical improvement" in task performance (Hartwigsen et al., 2015; Pascual-Leone, Walsh, & Rothwell, 2000). For instance, several studies reported faster response speed with different TMS protocols over a language area (Andoh et al., 2006; Nixon, Lazarova, Hodinott-Hill, Gough, & Passingham, 2004; Sliwinska et al., 2017; Sparing et al., 2001). Indeed, accounts of "state-dependent" effects of TMS posit that high-frequency rTMS does not necessarily have to lead to behavioral inhibition (Siebner, Hartwigsen, Kassuba, & Rothwell, 2009). It was argued that the TMS-induced activity or "neural noise" is not totally random (Ruzzoli, Marzi, & Miniussi, 2010). Depending on the neuron population that will be activated, the induced activity can be considered both as noise and as part of the task signal (Miniussi, Ruzzoli, & Walsh, 2010). The induced activity might be synchronized with the ongoing relevant signal, thereby rendering the signal stronger and providing an "optimum" level of noise for a specific task (Miniussi, Harris, & Ruzzoli, 2013). Moreover, factors like intensity and time point of stimulation as well as task difficulty have been shown to affect the behavioral outcome, particularly in online-paradigms like the one used here (Silvanto & Cattaneo, 2017). Consequently, the impact of a TMS-induced "lesion" effect might change with varying task conditions and complexity (Hartwigsen, Golombek, & Obleser, 2015). It has been argued that when TMS is applied to a region that is expected to be involved in a given task *before* the cognitive process is executed, the initial neuronal activation state of that region is altered (i.e., suppressed), causing divergent behavioral effects (Sandrini et al., 2011; Stoeckel, Gough, Watkins, & Devlin, 2009). During word production, phonological processing is assumed to take place at a rather late stage (Levelt, Roelofs, & Meyer, 1999). Therefore, for the majority of the trials, applying rTMS between 500 and 1,000 ms after stimulus onset may not have interfered with phonological processing yet, since mean naming latencies were at ~1,800 ms (range: 824–4,437 ms). Note that we initially chose this time point to cover a large time window during processing with our rTMS burst. However, instead of interfering with phonological processing, rTMS might have rather increased the amount of activity in the targeted pIFG to a level that was optimal for task performance, potentially resulting in a "pre-activation" of phonological activity (see Töpper, Mottaghy, Brügmann, Noth, & Huber, 1998; Sparing et al., 2001, for a similar reasoning). This explanation is supported by a number of previous studies that reported behavioral facilitation when single-pulse or high-frequency TMS was given immediately before picture naming over left-hemispheric language areas (Mottaghy et al., 1999; Sparing et al., 2001; Töpper et al., 1998; Wassermann et al., 1999). In contrast, behavioral accuracy was decreased when online rTMS bursts were applied *during* picture naming (i.e., later in time) over frontal or temporal language areas (Flitman et al., 1998; Wassermann et al., 1999). It would be most interesting to investigate whether the facilitatory effect can be reversed when TMS pulses are applied at a later time point (e.g., 1,000 ms after stimulus onset). Here, the use of a chronometric TMS approach that allows for disentangling the contribution of different sub-processes across the time-course of language production might be most promising. This would provide strong support for state-dependent theories within higher cognitive functions. Furthermore, we cannot rule out that this process is specific to language production and does not apply to other higher cognitive functions. Consequently, future studies should test whether similar or different result patterns are observed for other cognitive tasks (e.g., related to working memory or cognitive control). Such experiments could provide additional insights both in the mechanisms of TMS in modulating cognitive performance, and in the specific neurocognitive operations involved in language production.

Additionally, an interaction between stimulation intensity and task difficulty has been reported in the visual domain, such that suprathreshold TMS inhibited motion detection performance of easy targets, whereas subthreshold TMS facilitated motion detection of difficult targets (Schwarzkopf, Silvanto, & Rees, 2011). Given that we applied rTMS at subthreshold levels and the rhyming task was consistently more difficult than the category member generation task, the facilitatory effect may also be best explained within this framework. The fact that the observed facilitation effect on phonological response speed was task-specific and selectively occurred with rTMS over pIFG but not aIFG or vertex argues against an unspecific facilitation effect associated with the audio-tactile input of the stimulation (Duecker & Sack, 2013).

Regardless of the polarity of the effect, the current study shows that the left pIFG exhibits a functional specialization for phonological processing in word production. This is in line with previous neuroimaging research arguing for an involvement of this area in syllabification (de Zubicaray & Piai, 2019; Indefrey, 2011), but also underlines its role in phonological working memory (Perrachione, Ghosh, Ostrovskaya, Gabrieli, & Kovelman, 2017; Zurowski et al., 2002). Critically, by employing a rhyme production task, our study extends previous studies using phonemic fluency tasks, in which speakers are asked to name as many words as possible starting with a given letter. Here, we could show that the pIFG is indeed also recruited during the retrieval of word-final phonemes, as is required during rhyming.

Two additional issues need to be addressed. First, the phonological task consistently elicited higher error rates than the semantic task. Notably, worse performance in phonological as opposed to semantic fluency tasks has been reported in a number of previous studies (e.g., Cattaneo, Pisoni, & Papagno, 2011; Grogan, Green, Ali, Crinion, & Price, 2009; Meinzer et al., 2009; Vannorsdall et al., 2012). However, this difference was not critical for the current study, as our goal was not to directly contrast both tasks, but rather to investigate the influence of aIFG and pIFG separately for each process. In other words, we expected a modulation of behavior for only one task-by-region combination. Moreover, a difference in task performance at baseline was selectively found in the error rates, but not in the response latencies. This precludes a strong confounding influence of baseline differences between our tasks on the TMS-induced modulation of task-specific naming latencies in our study. Consequently, we are confident that differences in task difficulty did not affect our findings.

Second, a potential alternative explanation of our findings might be that TMS disrupted word comprehension rather than production in our study. However, we are confident that the current results cannot be attributed solely to an interference of TMS with word processing because we deliberately applied the pulses at a rather late onset. That is, by the time the pulses were given (i.e., starting at 500 ms after word onset and extending until 1,000 ms after word onset), processing of the visually presented words should have been largely completed already (Bentin et al., 1999; Pylkkänen & Marantz, 2003). The alternative explanation of a disruption of early word processing might be valid if participants deliberately delayed the processing of the stimulus until pulse onset. Given the automatic nature of word reading and processing, however, this seems unlikely.

In sum, our study provides first causal evidence for a functional double dissociation of semantic and phonological processing during language production in the left IFG, with the anterior region reacting selectively to semantic and the posterior region to phonological processing. The results shed light on the division of labor within this area and extend previous findings from the language comprehension domain. We believe that our findings may help to refine current models on the functional neuroanatomy of language production and might also help to increase the current understanding of specific language production difficulties associated with lesions of either the anterior or posterior part of the left IFG.

## ACKNOWLEDGMENTS

This work was supported by the German Research Foundation (KL 2933/3-1; HA 6314/3-1, HA 6314/4-1) and by the Max Planck Society. The authors would like to thank Ina Koch, Lisa Kunz, Laura Nieberlein, and Dana Richter for their assistance during data collection, and all volunteers for their participation.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Klaus J, Hartwigsen G. Dissociating semantic and phonological contributions of the left inferior frontal gyrus to language production. *Hum Brain Mapp*. 2019; 1–9. https://doi.org/10.1002/hbm.24597