Please Get to the Point! A Cortical Correlate of Linguistic Informativeness

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Abstract

■ The production of informative messages is an effortful endeavor that relies on the interaction between microlinguistic (i.e., lexical and grammatical) and macrolinguistic (i.e., pragmatic and discourse) levels of processing. Although the neural correlates of microlinguistic processing have been extensively studied, investigation of the ability to organize the macrolinguistic aspects of message production is scanty. In this article, we show that repetitive TMS of the dorsal portion of the anterior left, but not right, inferior frontal gyrus reduces the levels of lexical informativeness and global coherence of narratives produced by healthy individuals. Interestingly, levels of productivity and microlinguistic processing were unaffected by the stimulation. These results suggest that the dorsal aspect of the anterior left inferior frontal gyrus is an epicenter of a wider neural network subserving the selection of contextually appropriate semantic representations. ■

INTRODUCTION

Human language is a complex cognitive system that evolved to serve a specific function: the ability to exchange information in a very efficient way. However, the production of informative messages is an effortful endeavor, which requires the ability to select lexical representations that are appropriate to a given context and organize them within a communicative interaction avoiding unnecessary derailments (Marini, Boewe, Caltagirone, & Carlomagno, 2005; Nicholas & Brookshire, 1993). This ability relies on the interaction between several levels of representation (i.e., lexical, syntactic, pragmatic, and discourse ones) organized along two main dimensions (Marini, Andreetta, del Tin, & Carlomagno, 2011; Glosser & Deser, 1990). A microlinguistic dimension organizes phonemes into morphological strings and words (lexical processing) and determines the syntactic context required by each word for the generation of well-formed sentences (syntactic processing). A macrolinguistic dimension selects the contextually appropriate meaning of a word or a sentence (pragmatic processing) and connects utterances by means of cohesive and coherent ties to formulate the gist of a story or the main theme of a discourse, that is, its mental model (discourse processing).

In the past 20 years, a growing number of studies focusing on language processing unveiled the existence of an articulated cognitive architecture implemented in an extensive array of neural networks (Indefrey, 2011; Indefrey & Levelt, 2004). Although the neural correlates of lexical and grammatical processing have been extensively investigated (Vigneau et al., 2006), those underlying macrolinguistic (i.e., pragmatic and discourse level) processes have been much less explored. In particular, we are aware of only one study that explicitly assessed the neural correlates of the ability to select pragmatically adequate words from the mental lexicon (Spalletta et al., 2010). The authors found that, in a group of persons with schizophrenia, the production of lexical information units (LIUs; i.e., those words that had been appropriately selected and used from a phonological, grammatical, pragmatic, and textual point of view) significantly correlated with volume changes in the dorsal aspect of the left inferior frontal gyrus (lIFG). Even if this study provided only correlational evidence on the association between brain volume change in the lIFG and the ability to retrieve appropriate words in patients with mental disorders, this result is particularly interesting. Indeed, it suggests that this part of the lIFG may play a major role in a wider network for the controlled selection of contextually adequate words from the mental lexicon. Interestingly, in a single case study by Schwartz and Hodgson (2002), a patient with moderately severe transcortical motor aphasia due to hemorrhagic infarction of the left dorsolateral frontal cortex showed better word retrieval on standard naming tests than it was in her impoverished connected speech. Notably, neuroimaging evidence has implicated the lIFG in several language functions. Indeed, in two seminal papers, Blank et al. (Blank, Bird, Tukheimer, & Wise, 2003; Blank, Scott, Murphy, Warburton, & Wise, 2002) have explored connected speech production in both healthy individuals and patients with brain lesions. Namely, in a study focusing on healthy participants, Blank et al. (2002) identified in the lIFG an

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area activated in tasks of propositional speech production before articulation. Furthermore, this result was confirmed by a subsequent study where, during propositional speech, healthy individuals activated the left pars opercularis whereas activity in the right homologue was reduced relative to a baseline nonspeech condition. In the same study, a group of aphasic individuals with lesions to the left pars opercularis showed activation above baseline in the homologue area in the right hemisphere, thus pointing to the presence of a laterality shift of function during speech production from left to right pars operularis after infarction of the lIFG.

In a recent meta-analysis, Vigneau et al. (2006) showed an antero-posterior parcellation of areas within the lIFG, each specifically involved in phonological, syntactic, or semantic processing. Accordingly, TMS studies have shown that stimulation of distinct portions of the lIFG affects central linguistic functions (Devlin & Watkins, 2007), including performance on phonological (Nixon, Lazarova, Hodinott-Hill, Gough, & Passingham, 2004), syntactic (Cattaneo, Devlin, Vecchi, & Silvanto, 2009; Sakai, Noguchi, Takeuchi, & Watanabe, 2002), and semantic tasks (Whitney, Kirk, O'Sullivan, Lambon Ralph, & Jefferies, 2011; Hoffman, Jefferies, & Lambon Ralph, 2010; Köhler, Paus, Buckner, & Milner, 2004; Devlin, Matthews, & Rushworth, 2003). Devlin et al. (2003) demonstrated that repetitive TMS (rTMS) applied to the anterior lIFG significantly slowed the reaction times of a group of healthy participants on a semantic decision task. Moreover, a double dissociation has been demonstrated between stimulation of the anterior or posterior part of the lIFG and interference with semantic or phonological processing of words (Gough, Nobre, & Devlin, 2005). This result provided causative evidence in favour of an antero-posterior division of labor within the lIFG, where the anterior part of the lIFG, including the pars triangularis and orbitalis (BA 45/BA 47), is involved in semantic processing, and the posterior part, corresponding to the pars opercularis (BA 44), is involved in phonological processing.

To further explore the crucial role played by the lIFG in semantic processing and lexical retrieval in a discourse production task, we set out an experiment with an off-line rTMS protocol targeting at the area found correlated with the production of LIUs in Spalletta et al. (2010). Namely, we applied rTMS over a dorsal aspect in the anterior lIFG and right IFG (rIFG) at the border between the pars opercularis and the pars triangularis (BA 44/BA 45) and tested the effects of the stimulation on the narrative abilities of healthy individuals. We hypothesized that a selective reduction of the participants' informative skills after the stimulation of the lIFG (but not of the right IFG) would provide causative evidence of its role in the retrieval and selection of contextually appropriate semantic representations in a highly demanding task such as narrative production (Figure 1).

METHODS

Participants

Twelve native Italian-speaking participants (five women, all students at the University of Udine) aged 20–28 years (mean = 21.9 years, *SD* = 2.7 years) were recruited for the study. They were graduate students with at least 14 years of formal education (mean = 14.7 years, *SD* = 1.2 years). All participants were right-handed according to a standard handedness inventory (Briggs & Nebes, 1975) and reported normal or corrected-to-normal visual acuity in both eyes and no hearing loss. None of the participants had neurological, psychiatric, or other medical problems or any contraindication to TMS (Rossi, Hallett, Rossini, &

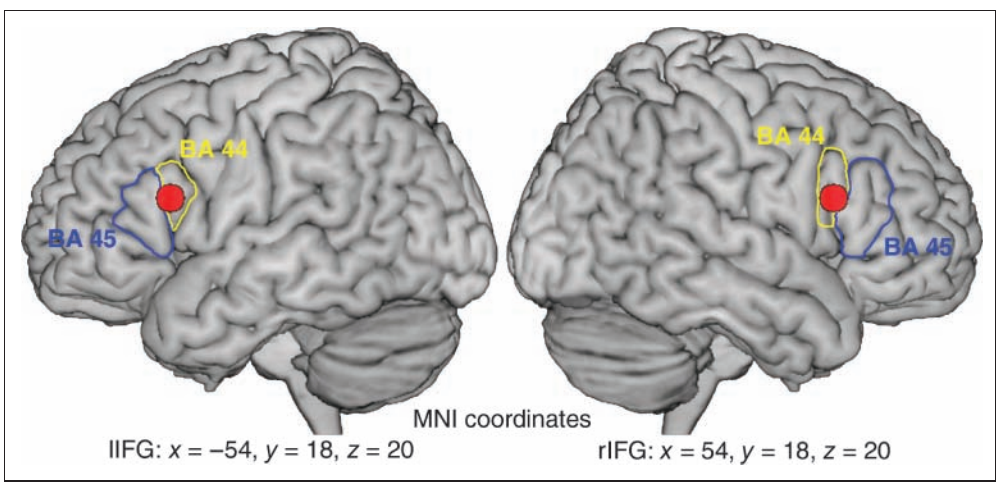

Figure 1. Schematic representation of the stimulation sites. Two 1-cm diameter ROIs (in red) were created on the brain template provided with the MRIcron software (www.cabiatl.com/mricro) around the voxel corresponding to the coordinates (reported in Montreal Neurological Institute space) of lIFG and rIFG. The indicative outlines of BA 44 (in yellow) and BA 45 (in blue) were also delineated on the brain rendering to facilitate localization of the stimulation sites as compared with previous studies. The scalp positions corresponding to the lIFG and rIFG target sites were searched with the Softaxic Neuronavigation system (EMS, Bologna, Italy).

Pascual-Leone, 2009). All participants released their written informed consent to participate in the study after all procedures had been fully explained. Approval for the study had previously been obtained from the ethics committee of the Scientific Institute (IRCCS) "E. Medea" (Bosisio Parini, Como, Italy), and the procedures were in accordance with the ethical standards of the 1964 Declaration of Helsinki. No painful sensations or adverse effects during rTMS were reported or noticed, and no participants wanted to interrupt the stimulation protocol for any major discomfort induced by the facial muscular twitches evoked by rTMS.

Assessment of Linguistic Abilities

The linguistic abilities of the participants in the three conditions were assessed by administering a phonemic fluency test, a task of picture stories arrangement, and a single picture and cartoon story description task. The order of administration of the three tasks was counterbalanced across participants. The phonological fluency task included the request to produce in 1 min as many words as possible beginning with a specific phoneme (two phonemes per condition). This test allows to derive a series of measures: productivity (i.e., number of words produced); number of phonological clusters produced (i.e., groups of words beginning with the same phonemes or ryiming with each other); phonological cluster size (i.e., number of words per phonological cluster); ratio of phonological cluster switching (i.e., number of switches from one phonological cluster to the other/the number of phonological clusters); number of semantic clusters produced (i.e., groups of words belonging to the same semantic field); semantic cluster size (i.e., number of words per semantic cluster); and ratio of semantic cluster switching (i.e., number of switches from one semantic cluster to the other/the number of semantic clusters).

In the cartoon stories ordering task, the participants were asked to arrange into a plausible sequence one unordered cartoon picture story per condition. They were made up of six pictures each and were given to the participants in random order. So, all participants arranged three cartoon stories. This allowed assessing their ability to generate (and eventually modify) a mental model incorporating the pictures into a coherent plot across the three conditions.

The assessment of narrative abilities was performed on storytellings. Each participant was asked to produce a total of six narratives elicited with the help of three single pictures depicting a shot of a story (the scene of a "Picnic" [Kertesz, 1982], the picture of the "Cookie Theft" [Goodglass & Kaplan, 1972], and the picture of "Smith's Family" [Nicholas & Brookshire, 1993]) and three vignettes with six pictures each presented on the same page (the stories of the "Flower Pot" [Huber & Gleber, 1982], "Quarrel" [Nicholas & Brookshire, 1993], and the "Nest Story" [Paradis, 1987]). Each participant told all six stories, but one single-shot picture and one cartoon story picture were presented in each experimental condition (no-rTMS; lIFG-rTMS, rIFG-rTMS). The association of the picture pairs to each experimental condition was counterbalanced across participants. Thus, for each participant different pictures were presented in the three conditions, but across participants all the pictures were equally presented in each condition. This avoided possible learning effects following the repetition of the same story and, at the same time, the spurious effects due to differences in the difficulty and type of narratives elicited by the six stories.

Each storytelling was tape-recorded and subsequently transcribed verbatim by two independent raters; the transcription included phonological fillers, pauses, false starts, and extraneous utterances. These transcriptions underwent quantitative, in-depth linguistic, and textual analysis focusing on four main aspects of linguistic processing: structural productivity, functional productivity, lexical encoding, and textual organization (see Marini, Andreetta, et al., 2011, for a thorough description of the procedure of transcription and analysis and Table 1 for a global description of the narrative measures).

Productivity measures included units, words, speech rate, and mean length of utterance (MLU). The unit count included each word, nonword, or syllabic false start uttered by the speaker. The total number of well-formed words with the exception of phonological fillers, phonemic paraphasias, and phonetic errors was then computed. The number of words was used to derive a measure of speech rate in terms of words per minute (words/min). For each story description, the total number of utterances was assessed following the criteria established in Marini, Andreetta, et al. (2011). MLU was calculated by dividing the total number of words by the number of utterances.

Lexical processing was assessed in terms of semantic, morphological, and phonological access. The speaker's ability to select semantically appropriate words (i.e., lexical-semantic processing) was analyzed in terms of his or her production of semantic paraphasias. When a target word was substituted by a semantically related word, a semantic paraphasia was counted. An example of semantic paraphasia is provided by the word "mother" in the sequence /here he's talking to his mother/, where the speaker implied "wife." Lexical-semantic processing was measured by the percentage of occurrences of semantic paraphasias on the total number of content words. Higher values represent more semantic errors per word. The speaker's ability to access morphological and morphosyntactic information relative to the selected word was assessed in terms of paragrammatic errors. These include grammatical errors with bound morphemes (e.g., /questo è una coppia [in English: "this [masculine] is a couple [feminine]"]/ where the pronoun *questo* ends with the wrong bound morpheme -o, which indicates masculine gender instead of the appropriate morpheme -a in agreement with the feminine word *coppia*) and function words (e.g., prepositions,

Table 1. Schema Showing the Microlinguistic and Macrolinguistic Measures Used in the Analyses of the Narrative Production Task

Microlinguistic analysis	
Productivity	
Words	Total number of well-formed words (i.e., all those units that were not scored as phonological errors).
Speech rate	Number of well-formed words produced in a minute.
MLU	The mean number of words that made up the utterances produced by each participant.
Lexical errors	
%Phonological errors	The percentage of units produced by each participant that were scored as phonological errors (i.e., false starts, phonological and phonetic paraphasias and neologisms).
%Semantic paraphasias	The percentage of words that were scored as semantic errors (e.g., semantic or verbal paraphasias). A semantic paraphasia consists in the substitution of a target word with another word, which can be either semantically related (e.g., "cat" instead of "dog") or unrelated (e.g., "table" instead of "chair").
%Paragrammatic errors	The percentage of words that were classified as paragrammatic errors. These include: the substitution of bound morphemes (i.e., "questo è una coppia" "this [masc in Italian] is a couple [fem]"—in Italian "questo" should be "questa") or function words (i.e., "batte da una porta" "he is knocking from a door"—in Italian "da" instead of "a").
Macrolinguistic analysis	
Informative content	
%Lexical informativeness	The percentage of words that were scored as LIUs, i.e., those words that were not only well formed from a phonological point of view but also grammatically and pragmatically accurate. This broad category includes all those words that were not scored as phonological errors, semantic paraphasias, or paragrammatic errors and were not ambiguous, repeated, or forming tangential utterances.
Textual organization	
%Local coherence errors	The percentage of utterances that were not accurately connected because they presented local coherence errors. Local coherence errors include the use of words with unclear referents and erratic topic shifts. An erratic topic shift occurs whenever an utterance is abruptly interrupted and in the subsequent utterance, instead of completing the preceding utterance, the speaker introduces a new topic.
%Global coherence errors	The percentage of utterances that violated global coherence rules. Global coherence refers to the conceptual connectivity across long-distant sentences within a discourse. Global coherence errors include the production of utterances that may be tangential, conceptually incongruent with the story, propositional repetitions or simple fillers.

conjunctions, or articles as shown in the following example: /batte da una porta [in English: /he is knocking from a door]/, where the wrong function word *da* has replaced the correct preposition *a*). The percentage of paragrammatic errors was calculated by dividing the total number of paragrammatic errors by the number of phonologically well-formed words and multiplying this value by 100. Therefore, higher values in the ratio of paragrammatisms in the connected speech samples represent more errors per word. Finally, the participants' ability to produce phonologically well-formed words was assessed computing a percentage of phonological errors. This was derived by dividing the total number of phonological errors (i.e., false starts, phonological and phonetic paraphasias, and neologisms) by the number of units and then multiplying this value by 100.

Macroelaborative processing was analyzed in terms of discourse organization that included the percentages of local and global coherence errors. The percentage of local coherence errors measured the extent to which each utterance of the narrative was conceptually related to the preceding one. Local coherence errors included the production of words without a clear referent and erratic topic switching. Missing referents were counted whenever the referent of a pronoun or the implicit subject of a verb was not unambiguously clear. For example, consider the following sequence of utterances: /Qui stanno litigando furiosamente/Poi dice/ (in English: /Here they are quarrelling furiously/Then [implicit pronoun] says/). In the second utterance, there is a missing referent because it is not clear whom the verb "dice" ("says") refers to. As to the second type of error of local coherence, that is, erratic topic switching, we did not score instances of "normal" topic shift (i.e., normal switches from one topic to another during the production of a narrative). Rather, an erratic topic switch was scored whenever an utterance was abruptly interrupted but the following utterance did not continue the flow of thoughts, therefore introducing new pieces of information. For instance, in the sequence: /he's trying to…/these two girls are watching the dog/, the first utterance remains unfinished while the second utterance introduces new information. The percentage of local coherence errors was calculated by dividing the number of local coherence errors by the number of utterances and multiplying this value by 100. Errors of global coherence included the production of utterances that may be tangential, conceptually incongruent with the story, propositional repetitions, or simple fillers. An utterance is considered tangential when it contains a derailment in the flow of discourse with respect to the information previously provided in preceding utterances. For instance, let's consider the following sequence produced during the description of the Picnic picture: /It is a picnic/I like picnics/I have made several picnics in my life/. Here, the second and the third utterances are scored as tangential, as they provide information that is irrelevant for the task and is simply triggered by a specific idea depicted in the stimulus. An utterance is considered conceptually incongruent when it includes ideas not directly addressed by the stimulus. Let's consider the following sequence produced by a speaker during the Cookie Theft picture description task: /the children are trying to get the cookies/ the TV is out/. In this example, the second utterance is scored as conceptually incongruent because in the picture stimulus there is no TV. A propositional repetition is a sequence where the speaker simply repeats ideas that he or she has already provided. Therefore, in these propositions the speaker does not add any new information. Let's consider the following example: /the man is walking on the sidewalk/he is on the sidewalk/. In this case, the second utterance simply repeats what has already been stated in the preceding one. Finally, a filler utterance is scored whenever the speaker produces an utterance that is not providing any additional information like in the following sequence: /the man and the woman are eating/my god, and now?/ah, yes, I get it/. The last two utterances are considered as filler utterances as they simply reflect a moment in narration when the speaker is simply thinking about the story and what to say next. The percentage of global coherence errors was calculated by dividing the number of global coherence errors by the number of utterances and multiplying this value by 100.

The functional productivity of each participant in each condition was evaluated in terms of the production of appropriate LIUs, that is, those words that were not only phonologically well formed but also appropriate from a grammatical and pragmatic point of view. Therefore, all those words that were classified as semantic paraphasias, fillers, paragrammatic errors, or forming tangential or extraneous utterances (i.e., utterances that were somehow deviating from the gist of the story) were excluded from the LIUs' count. A percentage of lexical informativeness was then obtained by dividing the number of LIUs by the number of phonologically well-formed words.

The scoring procedure was performed independently by the two raters on the 72 stories (six stories per subject, two per each of the three conditions) and then compared. The raters were blind with respect to the specific rTMS condition of the different stories. An interrater reliability analysis using the Kappa statistic was performed to determine consistency among raters (see Table 2). Acceptable interrater reliability was defined as $\kappa \geq .80$ (Carletta, 1996; Landis & Koch, 1977). As can be seen in Table 2, the interrater reliability scores for the two raters are constantly high. During the analysis in a few cases we needed to listen again to the audio recordings to face the residual minor issues that could be easily solved. The scores for each narrative presented in each rTMS condition were averaged, thus resulting in nine variables measured for each subject in three rTMS conditions.

Stimulation Procedure

An off-line rTMS stimulation protocol was adopted: Subjects performed the behavioral tasks after 15 min of low frequency (1 Hz; 900 pulses) rTMS stimulation applied over the lIFG and the rIFG as well as in a no-rTMS condition (see Figure 1). TMS pulses were delivered using a Magstim Rapid stimulator (Magstim Co., Whitland, UK) with a biphasic current waveform, producing a maximum output of 2 T at the coil surface (pulse duration, 250 μsec; rise time, 60 μsec), which was connected to an air-conditioned eight-shaped air-cooled coil (outer diameter of each wing, 7 cm). Before rTMS, motor threshold of the participants was estimated by releasing single

Table 2. Details of the Interrater Reliability Analysis Performed on the Narrative Analysis Conducted by Two Independent Raters Using the Kappa Statistic

Variable	*Cohen's κ*	*p*
Words	1.000	.000
Speech rate	1.000	.000
MLU	.986	.000
% Lexical informativeness	.901	.000
% Phonological errors	.940	.000
% Semantic paraphasias	.972	.000
% Paragrammatic errors	.1000	.000
% Local coherence errors	.936	.000
% Global coherence errors	.866	.000

magnetic pulses to the optimal scalp position for evoking motor-evoked potentials with maximal amplitude from the right first dorsal interosseous muscle (FDI). Electromyographic recordings from the FDI muscle were performed through surface Ag/AgCl cup electrodes (1-cm-diameter) placed in a belly-tendon montage. Responses were amplified, band-pass filtered (20 Hz to 2 kHz), and digitized by means of a Viking IV electromyography equipment (Nicolet Biomedical, Madison, WI). The sampling rate of the EMG signal was 20 kHz. A prestimulus recording of 80 msec was used to check for the presence of EMG activity before the TMS pulse. The resting motor threshold was defined as the lowest stimulus intensity able to evoke 5 of 10 motor-evoked potentials with an amplitude of at least 50 μV while holding the stimulation coil over the optimal scalp position for the FDI muscle. Resting motor threshold values varied from 40% to 66% (mean = 52.7%, *SD* = 7.8). During rTMS of both lIFG and rIFG, the stimulator output was set to an intensity of 90% of the individual resting motor threshold, thus reducing the possible discomfort and adverse effects of rTMS (Rossi et al., 2009) and the diffusion of neural alteration to distant sites (Speer et al., 2003).

The coordinates in the Montreal Neurological Institute space of the stimulation sites were $x = -54$, $y = 18$, $z = 20$ for lIFG and $x = 54$, $y = 18$, $z = 20$ for rIFG and were taken from the only previous neuroimaging investigation of macroelaborative linguistic functions with a storytelling task comparable to that used in the present study (Spalletta et al., 2010). These areas were located on each participant's scalp with the SofTaxic Optic—neuronavigation system for TMS (Electro Medical Systems, Bologna, Italy; www.softaxic.com). Skull landmarks (nasion, inion, and two preauricular points) and 60 points providing a uniform representation of the scalp were digitized by means of a Polaris Vicra optical tracking system (Northern Digital, Inc., Waterloo, Ontario, Canada). Coordinates in standard space were automatically estimated by the SofTaxic Otpic system from an MRI-constructed stereotaxic template, which also allowed on-line monitoring of the position of the coil focus over the target positions during stimulation. The coil was placed and securely held tangentially to the scalp by means of a coil holder, with the handle pointing backward and approximately parallel to the lateral sulcus. Immediately after the end of the rTMS train over lIFG and rIFG or in the no-rTMS condition, participants performed the storytelling, the phonological fluency, and the cartoon stories ordering tasks. The order of administration of the three tasks was counterbalanced between participants. Performing all the three tasks had a maximal duration of 9 min, thus within the time limit of the estimated effects of a 15-min, 1-Hz rTMS stimulation protocol (Chen, 1997). Completion of the task required about 4 min for the storytelling, 2 min for the phonological fluency, and 2 min for the cartoon stories ordering task. The interval between two consecutive stimulation conditions was at least 60 min, thus ensuring that any residual effect of rTMS had faded away (Avenanti, Annella, Candidi, Urgesi, & Aglioti, 2012; Whitney, Kirk, O'Sullivan, & Lambon Ralph, 2012; Whitney et al., 2011; Pobric, Jefferies, & Lambon Ralph, 2010; Lambon Ralph, Pobric, & Jefferies, 2009).

Data Analysis

The number of words produced in the phonemic fluencies task and the number of correctly ordered stories in the cartoon stories ordering task were analyzed. As for the storytelling task, the analysis focused on nine linguistic variables (words, MLU, speech rate, % LIUs, % phonological errors, % semantic paraphasias, % paragrammatic errors, % local coherence errors, % global coherence errors) across the three conditions. A series of one-way repeated-measures ANOVAs were performed to compare the performance of the 12 participants in the three tasks across the three conditions. The level of statistical significance for all ANOVA effects was set at $p < .006$ after Bonferroni correction for multiple comparisons (nine variables). To further explore condition-related differences, post hoc Tukey's tests were performed.

RESULTS AND DISCUSSION

Linguistic and Narrative Analysis

No significant condition-related difference was found either in the cartoon stories ordering task (the participants correctly arranged the same number of stories in each condition; $F(2, 18) = 1.53$, $p = .860$, $\eta_p^2 = 0.017$) or in the phonological fluency test (lIFG: mean = 25.8, *SD* = 6.9; rIFG: mean = 24.9, *SD* = 6.3; no-rTMS: mean = 25.2, *SD* = 6.6; $F(2, 18) < 1$, $p = .929$, $\eta_p^2 = 0.008$). Further analyses of the participants' performance on the phonological fluency test across the three conditions showed the absence of any condition-related difference in the number of phonological clusters (lIFG: mean = 5.8, *SD* = 2.6; rIFG: mean = 5.1, *SD* = 1.9; no-rTMS: mean = 4.8, *SD* = 2.5; $F(2, 18) < 1$, $p = .527$, $\eta_p^2 = 0.069$), in phonological cluster size (lIFG: mean = 2.4, *SD* = 0.4; rIFG: mean = 2.3, *SD* = 0.8; no-rTMS: mean = 3.3, *SD* = 2.3; $F(2, 18) = 1.562$, $p = .237$, $\eta_p^2 = 0.148$), and in the ratio of phonological cluster switching (lIFG: mean = 2.8, *SD* = 1.7; rIFG: mean = 3.6, *SD* = 2.7; no-rTMS: mean = 4.3, *SD* = 4; $F(2, 18) < 1$, $p = .985$, $\eta_p^2 = 0.002$). Similar analyses showed the absence of any condition-related difference in the number of semantic clusters (lIFG: mean = 3.3, *SD* = 1.2; rIFG: mean = 3, *SD* = 1.6; no-rTMS: mean = 3.6, *SD* = 2.2; $F(2, 18) < 1$, $p = .687$, $\eta_p^2 = 0.041$), in semantic cluster size (lIFG: mean = 2.3, *SD* = 0.3; rIFG: mean = 2.4, *SD* = 0.4; no-rTMS: mean = 1.9, *SD* = 0.7; $F(2, 18) = 2.109$, $p = .150$, $\eta_p^2 = 0.190$), and in the ratio of semantic cluster switching (lIFG: mean = 6.3, *SD* = 2.5; rIFG: mean = 8.4, *SD* = 5.6; no-rTMS: mean = 6.3, *SD* = 2.3; $F(2, 18) < 1$, $p = .488$, $\eta_p^2 = 0.077$).

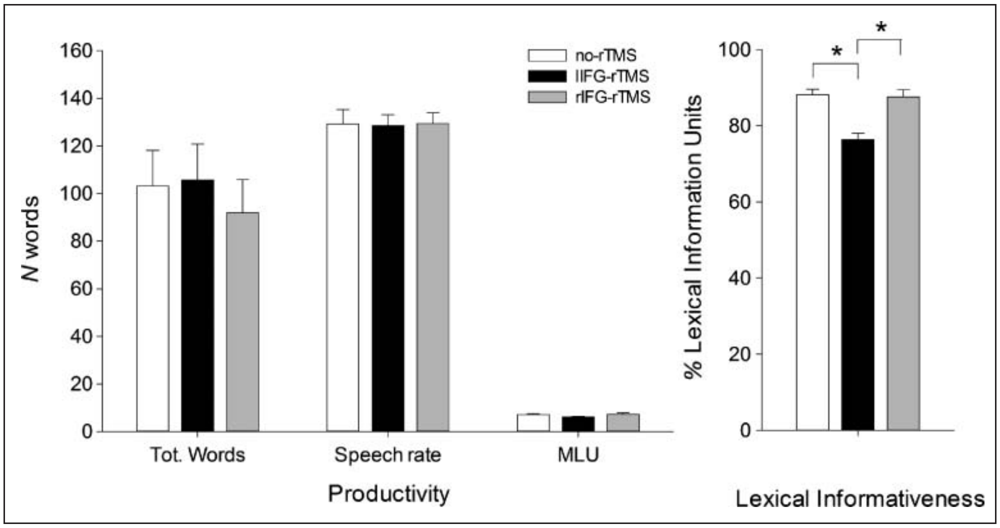

Figure 2. Effect of magnetic stimulation on structural and functional productivity. The graphs show the levels of structural and functional productivity in the three rTMS conditions: no-rTMS, rTMS of lIFG, and rTMS of rIFG. The measures of productivity included the total number of well-formed words (Tot. words), the number of well-formed words per minute (Speech rate), and the MLU. The measure of informativeness evaluated the production of appropriate LIUs (%LIUs), that is, those words that were not only phonologically well formed but also appropriate from a grammatical and pragmatic point of view. Asterisks (*) indicate significant difference between the three rTMS conditions after Bonferroni correction for multiple comparisons ($p < .006$).

The participants produced narratives with similar levels of productivity across the three conditions (Figure 2). Indeed, their story descriptions had similar lengths, words: $F(2, 22) = 1.74$, $p = .198$, $\eta_p^2 = 0.137$, and were uttered with comparable speech rates, $F(2, 22) < 1$, $p = .980$, $\eta_p^2 = 0.002$, and MLUs, $F(2, 22) = 3.76$, $p = .039$, $\eta_p^2 = 0.255$. Crucially, however, the informativeness of the participants' verbal productions was affected by rTMS, $F(2, 22) = 17.8$, $p = .000$, $\eta_p^2 = 0.618$, since participants produced significantly fewer LIUs (Figure 2) after lIFG-rTMS than after rIFG-rTMS ($p < .001$) and in the no-rTMS condition ($p < .001$), with nonsignificant difference between rIFG-rTMS and no-rTMS conditions ($p = .967$). Analyzing the specific types of errors involving the microlinguistic or the macrolinguistic levels of processing (Figure 3), we found nonsignificant differences across the three rTMS conditions in the production of phonological errors, $F(2, 22) < 1$, $p = .429$, $\eta_p^2 = 0.074$, semantic paraphasias, $F(2, 22) < 1$, $p = .395$, $\eta_p^2 = 0.081$, and paragrammatic errors, $F(2, 22) = 2.74$, $p = .087$, $\eta_p^2 = 0.199$. A different

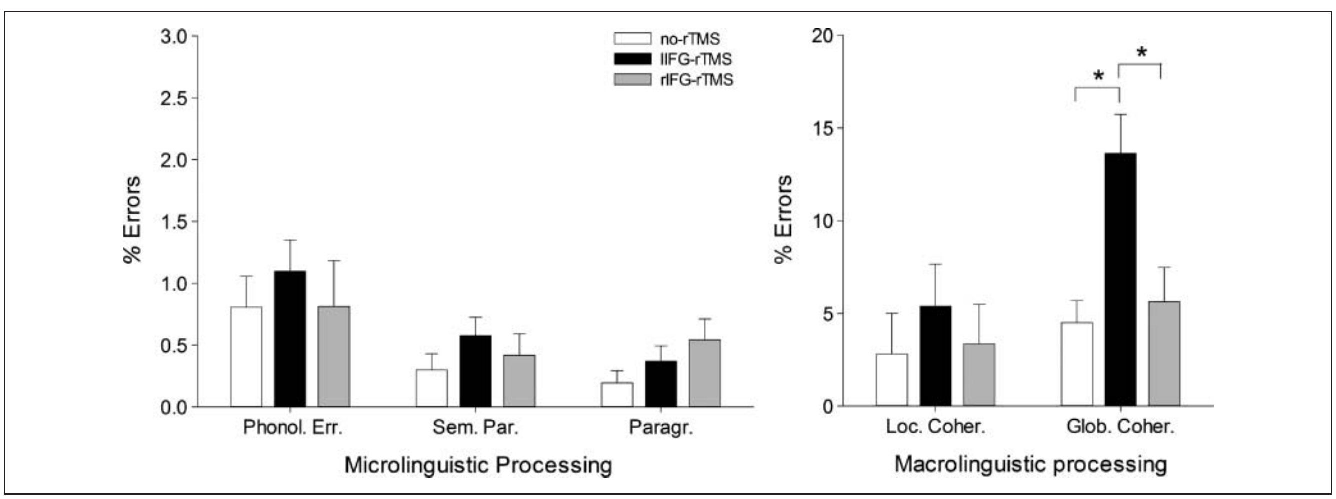

Figure 3. Effect of magnetic stimulation on micro- and macrolinguistic processing. The graphs show of the percentage of errors of lexical and macrolinguistic processing in the three rTMS conditions: no-rTMS, rTMS of lIFG, and rTMS of rIFG. The measures of microlinguistic processing included the percentage of phonological errors (Phonol. Err.), semantic paraphasias (Sem. Par.), and paragrammatic errors (Paragr.). The measures of macrolinguistic processing included the percentage of local (Loc. Coher.) and global coherence (Glob. Coher.) errors. Asterisks (*) indicate significant difference between the three rTMS conditions after Bonferroni correction for multiple comparisons ($p < .006$).

picture emerged from the analysis of the participants' macrolinguistic skills across the three conditions. Indeed, if no significant difference was found in the production of local coherence errors, $F(2, 22) = 2.89$, $p = .077$, $\eta_p^2 = 0.208$, a significant condition-related difference characterized the production of global coherence errors, $F(2, 22) = 11.97$, $p < .001$, $\eta_p^2 = 0.521$, with more global coherence errors in the lIFG-rTMS condition than in both the rIFG-rTMS ($p = .002$) and no-rTMS conditions ($p < .001$), which in turn did not differ from each other ($p = .845$). Thus, after lIFG rTMS, participants were less informative and produced more global coherence errors, while their productivity, lexical processing ability, and local coherence were unaffected by rTMS of either lIFG or rIFG. The estimated effect size of the change induced by lIFG-rTMS with respect to the no-rTMS condition showed huge effects for both LIUs (Cohen's $d = 2.24$) and global coherence errors (Cohen's $d = 1.62$). Thus, the participants' macrolinguistic skills were about 2 *SD* below their baseline performance.

Relationship between the Production of Violations of Global Coherence and Informativeness

The relationship between the production of violations of global coherence and informativeness was investigated

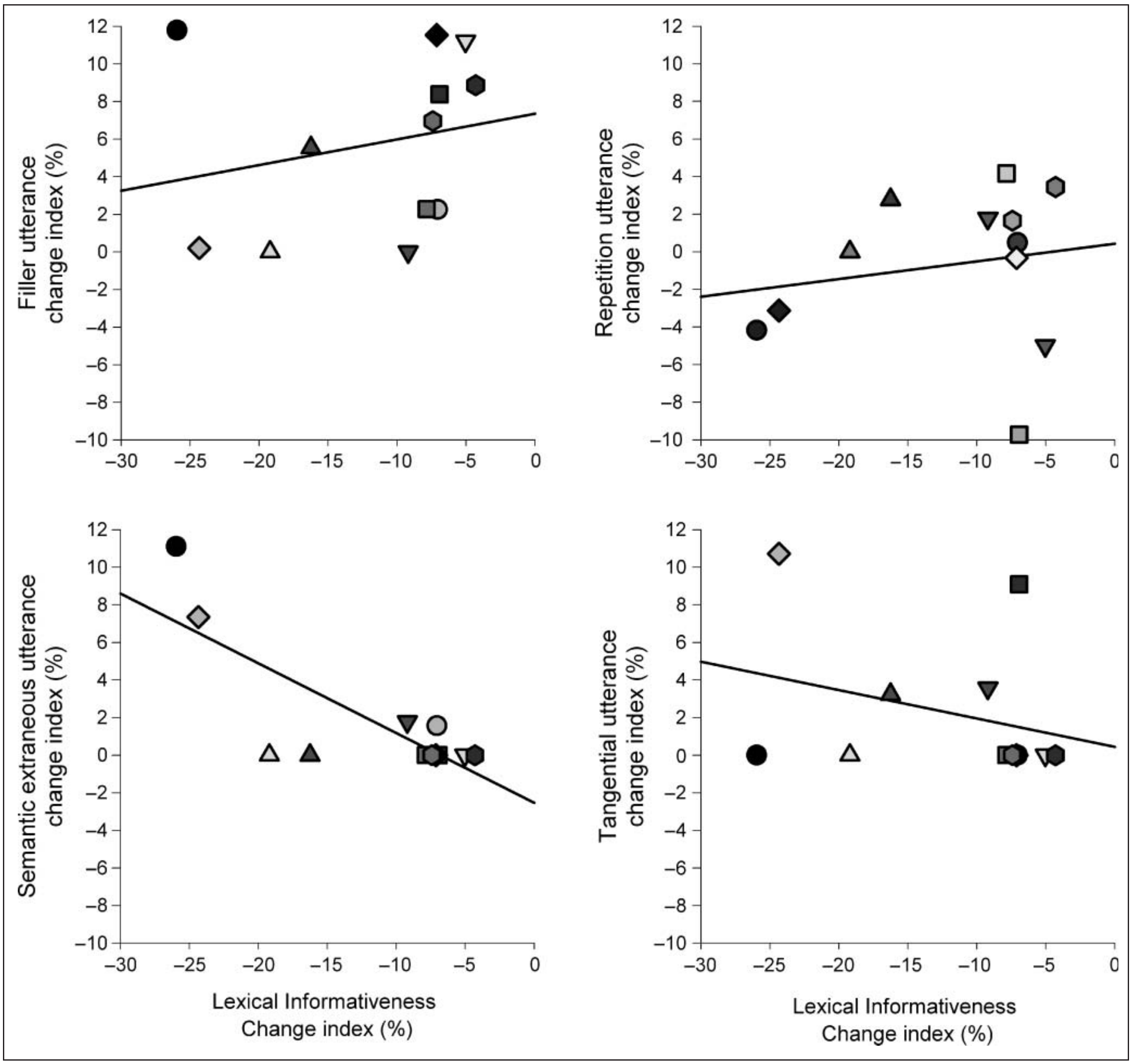

Figure 4. Correlation between lexical informativeness and global coherence errors. The scatterplot graphs show the correlation between the reduction of lexical informativeness after stimulation of the lIFG and the relative increase of each type of global coherence errors: filler, repetition, tangential, and semantically extraneous utterances.

by computing the Pearson product–moment correlation coefficients between the two measures in the lIFG-rTMS and no rTMS condition. The two variables showed a significant negative correlation after lIFG-rTMS ($r = -.667$, $p = .018$), showing that individuals with lower lexical informativeness also made more of violations of global coherence. A nonsignificant negative correlation between the two measures was also observed in the no-rTMS condition ($r = -.267$, $p = .402$), which was likely masked, however, by the low number of errors made by healthy participants at baseline. To further explore the specific types of errors that contributed to the poorer lexical informativeness after rTMS over lIFG, we calculated the change indexes for % LIUs and % utterances leading to global coherence violations: filler, repetition, tangential, and semantically extraneous utterances (see Methods section). The indexes were calculated by subtracting the percentage values of LIUs or of each type of global coherence errors during lIFG-rTMS from the percentage values of LIUs or of each type of global coherence errors during the no-rTMS condition. The change indexes for the four types of global coherence errors were entered as predictors into a standard multiple regression model with the change index for % LIUs as dependent variable (Figure 4). The whole model was marginally significant (adjusted $R^2 = .517$, $F(4, 7) = 3.94$, $p = .055$), with only the change in the number of semantically extraneous utterances resulting a significant predictor ($\beta = -.79$, $t(7) = -3.57$, $p = .009$). The change indexes in the number of filler, repetition, and tangential utterances filler were, instead, nonsignificant as predictors (all ps $> .37$).

Discussion

The rTMS of the dorsal portion of the lIFG did not affect phonological or morphological processing. However, it selectively reduced the levels of lexical informativeness while increasing the production of global coherence errors. Furthermore, the increased production of only one kind of global coherence errors (i.e., semantically extraneous utterances) predicted the reduction of lexical informativeness. These results can be interpreted as direct evidence of the important role played by the dorsal portion of the lIFG in the process of selection of contextually adequate conceptual representations.

According to current psycholinguistic models, message production (Indefrey & Levelt, 2000) is a multistage process (a phase of prelinguistic conceptual planning followed by phases of linguistic formulation and expression). Of particular interest here are the former two stages. In the prelinguistic conceptual phase, the speaker is assumed to generate a mental model of the intended message by integrating what he or she wants to say with what has been previously said (linguistic context), together with the particular situation, place, and time in which the communicative exchange takes place (extralinguistic context; Levinson, 1983). This way, the speaker modulates the amount of information that he or she intends to communicate and its relevance with respect to what has been previously said (Sperber & Wilson, 1986; Grice, 1975). Eventually, this conceptual information triggers the generation of appropriate propositions that must be organized at the macrolinguistic level by means of adequate cohesion and coherent links. In the phase of linguistic formulation, this preverbal message must be converted into a speech plan through a multistage process that entails a phase of lexical selection and one of lexical access. The former allows speakers to select the lexical representations that correspond to the intended meanings, whereas the latter allows them to retrieve their morphosyntactic and morphological features (lemma level of word representation) as well as their syllabic and phonological forms (Levelt, Roelofs, & Meyer, 1999).

Accordingly, the reduction of lexical informativeness after stimulation of the lIFG may be explained in terms of an interference at one of two levels of language processing. One possibility is that the stimulation of lIFG altered the ability to formulate a correct semantic representation of the story (i.e., its mental model), leading to the production of utterances conceptually incongruent with the target stimulus. This may have lowered the informative levels of these narrative descriptions. However, this possibility does not seem plausible. Indeed, in the picture arrangement task, the stimulation of the lIFG did not hamper the ability to generate a correct mental model for each picture story. This suggests that the connection between reduced levels of lexical informativeness and increased production of semantically extraneous utterances after rTMS of the lIFG does not likely reflect a temporary impairment in the process of mental model generation. Furthermore, investigations on the narrative skills of persons with neurological or psychiatric disorders (e.g., traumatic brain injury or schizophrenia; e.g., Marini, Galetto, et al., 2011; Marini et al., 2008) suggest that the most important marker of an inability to generate a correct mental model is the production of tangential utterances. However, even in the lIFG-rTMS condition, our participants produced just few errors of this kind. Overall, these considerations suggest that rTMS of the lIFG did not affect the ability to organize the mental model of the stories they were asked to describe. A more plausible interpretation of these results may be that rTMS of the lIFG hampered the selection of specific lexical concepts forcing the speakers to change the flow of discourse without arresting it (speech rate did not change after lIFG) so to occasionally produce utterances conceptually incongruent with the story. Speakers may have perceived an arrest of speech and a prolonged pause as more irritating or annoying than simply switching to a completely different argument. Therefore, we may interpret this as a strategy to cope with the increased perception of difficulties in selecting the right concepts. Interestingly, this interpretation is coherent with recent reports where anterior and posterior portions of the left inferior frontal cortex have been postulated to be important for the top–down controlled retrieval of concepts and the subsequent selection of highly activated candidates, respectively (Schuhmann, Schiller, Goebel, & Sack, 2012; Kim, Karunanayaka, Privitera, Holland, & Szaflarski, 2011; Lau, Phillips, & Poeppel, 2008).

Increasing neuropsychological, neuroimaging and rTMS evidence suggests that the lIFG is involved in the executive control of the access to semantic representations (e.g., Whitney et al., 2011; Wagner, Pare-Blagoev, Clark, & Poldrack, 2001). Persons with aphasia following stroke in the lIFG show specific semantic disturbances. They have difficulties in selecting the correct response in situations characterized by strong competition between potential alternatives that increases the need for semantic selection. This can be seen in tasks where they are required to complete sentences with low versus high predictive endings (Novick, Kan, Trueswell, & Thompson-Schill, 2009; Robinson, Shallice, & Cipolotti, 2005; Thompson-Schill et al., 1998) or must retrieve the subordinate meanings of ambiguous words struggling to reject highly associated distracters in synonim judgment tasks (Noonan, Jefferies, Corbett, & Lambon Ralph, 2009). Interestingly, they profit from cues provided to reduce the requirement for internally generated semantic control (e.g., /t/ to cue "tiger" during picture naming; Jefferies, Patterson, & Lambon Ralph, 2008). This suggests that these patients do not show degradation of semantic knowledge per se and their semantic difficulties relate to the control demands of the task. Thus, in contrast to patients with semantic dementia who have bilateral anterior temporal lobe degradation and exhibit progressive dissolution of semantic knowledge itself (Patterson, Nestor, & Rogers, 2007; Jefferies & Lambon Ralph, 2006; Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000), persons with stroke at the lIFG and semantic disturbances have intact semantic knowledge but impaired semantic control. Neuroimaging studies have further contributed to delineate the functional role of the lIFG in semantic executive control. Indeed, lIFG shows greater activation in semantic relative to phonological judgments (Devlin et al., 2003; Poldrack et al., 1999) and when semantic tasks that require high control demand are contrasted with those that require less control (Whitney, Grossman, & Kircher, 2009; Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Noppeney, Phillips, & Price, 2004; Gold & Buckner, 2002; Wagner et al., 2001; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997). In particular, neural activity of the dorsal aspect of the anterior lIFG (BA 44/BA 45), at the border between the pars opercularis and the pars triangularis, is modulated by the manipulation of the number of possible alternatives of the responses or by the need to associate words on the basis of specific versus global similarity (Badre et al., 2005). The dorsal aspect of the anterior lIFG may, thus, play a specific role in the selection of competing semantic information (Badre & Wagner, 2007). Conversely, neural activity in the ventral aspect of the anterior lIFG (BA 47), corresponding to the pars orbitalis is particularly modulated by the strength of association between two words and may be specifically involved in the controlled retrieval of semantic information when automatic activation of a concept and its related concepts are not enough to access the appropriate information. It should be noted, however, that the involvement of these regions may not be limited to the verbal component of conceptual processing. Rather, it may extend also to other domains, as suggested by evidence from imaging and patient studies on nonverbal semantic tasks including figure or gesture association (e.g., Visser, Jefferies, & Lambon Ralph, 2010; Binder, Deasi, Graves, & Conant, 2009; Corbett, Jefferies, Ehsan, & Lambon Ralph, 2009; Jefferies & Lambon Ralph, 2006; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996).

A few rTMS studies have recently provided causative evidence in favor of the involvement of the anterior lIFG in semantic control (Whitney et al., 2011, 2012; Hoffman et al., 2010). In all these studies, TMS was applied to the dorsal aspect of the anterior lIFG, in a location overlapping to the left hemisphere site targeted in the present study and corresponding to the area whose activation is sensitive to the manipulation of selection but not of controlled retrieval demands in fMRI studies (Badre & Wagner, 2007). Under the assumption that accessing the meanings of abstract words requires more executive regulation because of their variable, context-dependent meanings, Hoffman et al. (2010) reported that lIFG rTMS slowed comprehension of abstract but not concrete words. Importantly, in keeping with the performance of semantic aphasia patients, lIFG rTMS had detrimental effects only when abstract words were presented out of context, whereas it had no effect when words were preceded by a contextual cue that reduced the executive demands of the task. This result suggests that the dorsal aspect of the anterior lIFG plays an executive regulation role in abstract word processing when several alternatives must be discerned to select the most appropriate semantic information. More recently, Whitney et al. (2011, 2012) showed that rTMS to the same area impaired performance on a word sample-to-matching task that had high selection (feature vs. global similarity) and controlled retrieval (strong vs. weak associates) demands. Conversely, no lIFG rTMS effects could be detected when the matching could be performed on the basis of strong, automatic associations. All in all, these studies suggest a specific role of anterior lIFG in the controlled access and selection of semantic representations.

In conclusion, our data support the hypothesis that the dorsal portion of the anterior lIFG is an epicenter of the network subserving the process of controlled semantic selection. Furthermore, this study showed that structural and functional procedures of narrative discourse analysis can be of valuable importance for future studies aimed at generating updated models of human language processing at both cognitive and anatomo-functional levels. Finally, since rTMS of the lIFG has been increasingly used in the rehabilitation of patients with language disorders (Berthier

& Pulvermüller, 2011), a better understanding of the different levels of language process that are affected by stimulation of distinct portions of the lIFG may help to further specify the treatment protocols according to the patient's deficit pattern.

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