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Left Posterior Inferior Frontal Gyrus is Causally Involved in Reordering During Sentence Processing

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Abstract

Storage and reordering of incoming information are two core processes required for successful sentence comprehension. Storage is necessary whenever the verb and its arguments (i.e., subject and object) are separated over a long distance, while reordering is necessary whenever the argument order is atypical (e.g., object-first order in German, where subject-first order is typical). Previous neuroimaging work has associated storage with the left planum temporale (PT), and reordering with the left posterior inferior frontal gyrus (pIFG). Here, we tested the causal role of the PT and pIFG in storage and reordering using repetitive transcranial magnetic stimulation (rTMS). We applied either effective rTMS over PT or pIFG, or sham rTMS, while subjects listened to sentences that independently varied storage demands (short vs. long argument–verb distance) and reordering demands (subject– vs. object-first argument order). We found that rTMS over pIFG, but not PT, selectively affected reordering during the processing of sentences with a long argument–verb distance. Specifically, relative to sham rTMS, rTMS over pIFG significantly increased the performance difference between object– and subject-first long-distance sentences. These results demonstrate a causal involvement of left pIFG in reordering during sentence comprehension and thus contribute to a better understanding of the role of the pIFG in language processing.

Keywords: Broca's area, planum temporale, syntax, working memory, Transcranial Magnetic Stimulation

1 Introduction

During language comprehension, the core meaning of a sentence—who is doing what to whom—is established by linking the main verb to its arguments, consisting of the subject and object(s) (Frege, 1879; Heim and Kratzer, 1998). The linking of arguments and verb can be impeded by an increased argument–verb distance (Babyonyshev and Gibson, 1999; Cowper, 1976; Gibson, 2000; Grodner and Gibson, 2005), and an atypical argument order (e.g., object-first order in German or English; Friederici et al., 2006; King and Just, 1991). Thus, both long argument–verb distances and atypical argument orders can substantially increase processing demands. On the one hand, long argument–verb distances require the storage of arguments in working memory until their verb is encountered, so that arguments and verb can be linked (Fiebach et al., 2001; Kluender and Kutas, 1993; Meyer et al., 2013). On the other hand, atypical argument orders are associated with the reordering of arguments into the typical order (e.g. subject-first order in German or English), the order in which arguments are linked to their verb (Just and Carpenter, 1992; Kintsch and van Dijk, 1978; Meyer and Friederici, 2015).

For instance, the German sentence “Darum hat *den Autor der Leser* nach der Präsentation auf der Buchmesse *eingeladen*” (“Therefore has *the author [object] the reader [subject]* after the presentation at the book fair *invited [main verb]*”) requires both storage and reordering. The sentence’s subject “der Leser” and object “den Autor” are separated from their verb “eingeladen” by a prepositional phrase (“nach der Präsentation auf der Buchmesse”). Consequently, they are stored in working memory across the argument–verb distance. Additionally, because the argument order differs from the typical order, the arguments need to be reordered before they are finally linked with their verb.

A number of previous neuroimaging studies investigated the neural correlates of storage and reordering. Across these studies, the posterior inferior frontal gyrus (pIFG; Brodmann area 44) was consistently activated for atypical versus typical argument orders

(Ben-Shachar et al., 2003; Friederici et al., 2006; Kim et al., 2009; Meyer and Friederici, 2015). In contrast, the left temporo-parietal cortex was engaged in the short-term storage of verbal material (Kim et al., 2002; Novais-Santos et al., 2007; Owen et al., 2005; Smith and Jonides, 1998). In a previous neuroimaging study that independently manipulated both reordering and storage demands, Meyer et al. (2012a) found reordering demands (atypical, as compared to typical, argument order) to activate the left pIFG, whereas storage demands (long, as compared to short, argument–verb distance) increased activity of left temporo-parietal regions, with the activation peak located in the planum temporale (PT).

While these results provide evidence for a functional neuroanatomical dissociation of reordering and storage, correlative neuroimaging methods cannot determine whether a region is necessary for a particular cognitive function (Price and Friston, 2002). It is thus unknown whether the left pIFG and PT are indeed causally relevant for reordering and storage, respectively—or whether they are involved in activation that is incidental to task performance (i.e., redundant processing, cf. Price and Friston, 2002).

The causal relevance of a given cortical region for a certain function can be determined by repetitive transcranial magnetic stimulation (rTMS) applied during the task of interest (“online”) (Hartwigsen et al., 2015a; Pascual-Leone et al., 2000; Siebner et al., 2009; Walsh and Cowey, 2000). Although the precise physiological mechanisms underlying a TMS-induced disruption of a specific function are unclear, it is likely that online rTMS induces “neural noise” in the stimulated area that interferes with ongoing task-relevant activity and thereby impairs performance (Miniussi et al., 2010; Ruzzoli et al., 2010).

Here, we used online rTMS to probe the functional relevance of the left pIFG and PT for reordering and storage. rTMS was applied either over left pIFG or PT, or as ineffective sham-stimulation, while subjects listened to German sentences that systematically varied both the argument order (taxing reordering, presumably subserved by the pIFG) and argument–verb distance (taxing storage, presumably subserved by the PT). We expected online rTMS to

disrupt language processing in our study because a number of previous studies reported impairments in language comprehension with this protocol (e.g., Devlin et al., 2003; Gough et al., 2005; Hartwigsen et al., 2016, 2010a, 2010c).

In addition to determining causality in the functional-anatomical dimension, we aimed to extend Meyer et al.'s (2012a) findings by timing information as their methodology did not allow to pinpoint the critical times where pIFG and PT become involved in reordering and storage, respectively. This information can be provided by TMS applied at different time points during the task. It was previously argued that storage becomes crucial when the arguments are encoded in working memory (Meyer et al., 2013). Reordering, on the other hand, seems to take place at the verb (Meyer et al., 2012b; Nicol and Swinney, 1989). Therefore, rTMS was applied either early—during argument encoding in long-distance sentences (presumably disrupting storage), or late—on the verb (presumably disrupting reordering).

rTMS-induced disruption of sentence comprehension was assessed with a drift diffusion model (Ratcliff, 1978), which represents a powerful statistical tool to analyze data from binary decision tasks, and has already been successfully applied to model the behavioral effects of TMS (cf. Hartwigsen et al., 2015a; e.g. Georgiev et al., 2016; Philiastides et al., 2011; Soto et al., 2012).

Based on the results of Meyer et al. (2012a), we hypothesized to find a functional-anatomical double dissociation. Hence, rTMS over pIFG should selectively disrupt reordering, but not storage. That is, comprehension performance should selectively decrease for object–, as compared to subject-first, sentences. rTMS over PT, on the other hand, should selectively disrupt storage, and not reordering. Here, performance should selectively decrease for long–, as compared to short-distance, sentences. These effects should critically depend on the timing of the TMS pulses: Early TMS (applied during argument encoding in long-distance

sentences) should selectively interfere with the storage of incoming information, while late TMS (applied with verb onset) should only affect reordering.

2 Materials and Methods

2.1 Subjects

Data from 24 native German speakers (13 females, mean age = 26.96 years, standard deviation (SD) = 3.34) were analyzed. Initially, 31 participants had been recruited, but 7 subjects were excluded from further analyses because they experienced discomfort with the stimulation procedure. All subjects were recruited via the subject database of the Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany. All subjects were right-handed (Oldfield, 1971; mean laterality quotient = 94.41, SD = 7.13) and had no history of psychiatric, neurological, or hearing disorders. Each participant was paid 8 € per hour of participation. 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 of the University of Leipzig, Germany.

2.2 Experimental Procedures

The study used a 3 x 2 x 2 x 2 within-subjects factorial design with the factors TMS-SITE (pIFG, PT, sham), TMS-TIME (early, late), argument ORDER (subject-first, object-first), and argument-verb DISTANCE (short, long).

The experiment consisted of three TMS sessions (one for each TMS-SITE level), separated by at least 7 days (mean inter-session interval = 7.83 days, SD = 4.04 days) to prevent carry-over effects of TMS and minimize learning effects. Session order was counterbalanced across participants (to the degree possible due to exclusion of some participants).

Fig. 1A shows the timeline of one experimental session. All sessions comprised two runs of 128 trials each. Breaks between runs were used for coil cooling and adjustment, if necessary. Each run was split into two blocks of 64 trials. Prior to the first run, subjects practiced with 10 demo-trials (5 without and 5 with TMS), which were not included in the actual experiment. Total duration of each experimental session including preparation and neuronavigation (see below) was approximately 110 minutes.

Stimuli were presented using the software program *Presentation* (Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com). Questions were visually presented on an *EIZO* 19" LCD monitor positioned ~1–1.5 meters in front of the participant. Auditory stimuli were played via *Shure* SE215 sound isolating earphones, which simultaneously shielded the subject against the TMS-induced noise. Sound volume was individually adjusted during the demo trials.

Figure 1 here (Double column).

Fig. 1B depicts the timeline of a single trial of the experiment. Each trial began with a fixation cross shown on the screen, followed by the presentation of an auditory German sentence. Four types of sentences were created, which systematically and independently manipulated the argument order and argument–verb distance (Figure 2A; see Stimuli): (1) subject-first short-distance; (2) subject-first long-distance; (3) object-first short-distance; (4) object-first long-distance. During sentence presentation, 5 pulses of 10 Hz repetitive TMS (rTMS) were applied either (1) early (i.e., on the first word following the auxiliary verb) or (2) late (i.e., on the main verb). After stimulus presentation, a visual comprehension question was presented on the screen (Figure 2B; white letters, font: Verdana, font size: 16 px; gray background), which subjects had to answer within 4 seconds by pressing a button on a response-box. Response button assignment was counterbalanced across subjects. Finally, participants

received visual feedback with a happy or sad emoticon for a correct or false answer, respectively. Subsequently, the next trial was presented. Average trial duration ranged from 9.2 to 15.8 seconds. Response times (measured from question onset) and accuracy were measured for each trial.

2.3 Stimuli

96 different sets of sentences were created in the four conditions (i.e., subject-first short distance, subject-first long distance, object-first short distance, object-first long distance), resulting in a total number of 384 stimuli. To avoid potential semantic preferences to confound the experimental manipulations, the same sentences were produced with switched argument roles. That is, the subject of the first set of sentences became the object of the second, and vice versa, leading to a final stimulus pool of 768 stimuli. To further avoid confounding of the ORDER factor, subject and object of each sentence were matched in full word and lemma frequency and length (i.e., number of syllables) using the CELEX database (Baayen et al., 1995). Semantic coherence of each sentence's verb–argument combination was matched via sentential neighborhood analysis (Biemann et al., 2004; for a similar procedure, see Meyer et al., 2012a).

Three types of comprehension questions were presented (Figure 2B): (1) subject-first, (2) object-first, and (3) prepositional phrase control questions. Question types 1 and 2 were to be answered “no” when the assignment of subject and object was switched (e.g., Fig. 2B, 2). Question type 3 was to be answered “no” when the prepositional phrase of the comprehension questions did not match the prepositional phrase of the stimulus (e.g. Fig. 2B, 3). Question type 3 served to focus participants on memorization of the entire sentence instead of allowing them to solve the task by memorizing subject and object only.

Stimuli were recorded by a professional male German speaker in a soundproof chamber using a *Sennheiser* MKH 40 condenser microphone. *Praat* software (Boersma, 2002) was used to cut and normalize each recording to the root mean square amplitude of all stimuli. To remove acoustic edge artifacts, a cosine fade of 50 ms was added at the recording edges. For stimulation, 72 lists of 128 stimuli each were created in *Matlab* (The MathWorks, Inc., Natick, MA, USA). Stimuli were drawn in a pseudo-randomized and counterbalanced way from the stimulus pool. As it was impossible to fully balance QUESTION-TYPE in each list and subject, QUESTION-TYPE was balanced to the best extent possible both within and across subjects. The 72 lists were randomized over participants.

2.4 Transcranial Magnetic Stimulation

To investigate the critical contribution of left pIFG and PT to reordering and storage, we applied short trains of 10 Hz rTMS *during* the task (“online”). The main advantage of online rTMS relative to the application *before* a task (“offline”) is the more precise timing of the interference that allows for measuring its acute and transient consequences (Siebner et al., 2009). While common offline rTMS protocols can induce adaptive changes in brain activity and connectivity that may outlast the stimulation period for up to 30-50 minutes depending on the particular protocol (Siebner and Rothwell, 2003; Wischniewski and Schutter, 2015), the effects of short online rTMS bursts are too short-lasting to elicit adaptive reorganization (Hartwigsen et al., 2015a; Pascual-Leone et al., 2000; Walsh and Cowey, 2000). In particular, high-frequency online rTMS bursts typically affect cortical activity at the stimulated area for a period outlasting the stimulation for about half the duration of the stimulation train (Rotenberg et al., 2014), and thus provide a temporal resolution in the range of hundreds of milliseconds (Bergmann et al., 2016; Devlin and Watkins, 2008). Therefore, we are confident

that online rTMS should allow to assess at which point in time the stimulated areas crucially contribute to reordering or storage.

2.4.1 Neuronavigation

We used stereotactic neuronavigation (“TMS Navigator”, Localite GmbH, Sankt Augustin, Germany) to guide individual coil placement and maintenance of the exact location and orientation throughout the experiment. To this end, the subject’s head was co-registered onto their T1-weighted MR image at the beginning of each experimental session. T1-scans had been obtained beforehand with a 3-Tesla *Siemens* TIM TRIO scanner (Siemens Healthcare, Erlangen, Germany) using a magnetization-prepared rapid gradient echo (MPRAGE) sequence in sagittal orientation (inversion time = 650 ms, repetition time = 1300 ms, flip angle = 10°, field of view = 256 mm x 240 mm, voxel-size = 1 mm x 1 mm x 1.5 mm). Mean stereotactic coordinates for rTMS sites (Figure 2C) were derived from the group activation peaks for reordering in the left pIFG (MNI: x, y, z = -54 14 13 mm) and storage in the left PT (MNI: x, y, z = -42 -40 10 mm) reported previously (Meyer et al., 2012a). To precisely target these coordinates in each individual subject, they were transferred from standard to individual subject space for each participant (cf. Hartwigsen et al., 2016, 2010b) with the SPM8 software package (Wellcome Trust Center for Neuroimaging, University College London, UK). Note that stereotactic neuronavigation based on functional activation peaks yields a high spatial accuracy in the range of a few millimeters (Hartwigsen et al., 2010b; Sparing et al., 2008), and thus represents the current method of choice for precise positioning and monitoring of the coil (Neggers et al., 2004; Sack et al., 2006).

The coil was fixed over the target area using a tripod-arm (*Manfrotto* 244, Cassola, Italy) and adjusted during the experiment if it moved over 3 mm away from the target location. The coil-position was always optimized during breaks in-between blocks. For sham-stimulation, an additional coil was placed in a 90° angle above the first coil. Only the second

coil was charged. This ensured that the TMS-pulses produced an acoustic stimulus identical to the one during effective stimulation without actually stimulating the brain. The uncharged coil was navigated to the primary motor cortex (M1), so that the neuronavigation procedure did not differ between the sham session and the other sessions. To this end, mean stereotactic coordinates for M1 (MNI: x, y, z = -37 -21 58 mm) were derived from a previous meta-analysis (Mayka et al., 2006) and transferred to individual space (see above).

2.4.2 Stimulation Parameters

A MagPro X100 stimulator (MagVenture 4.3.20, Medtronic, Fridley, MN) equipped with a focal figure-of-eight coil (C-B60; outer diameter = 7.5 cm) was used for TMS application. The coil was oriented 45° to the sagittal plane, such that the second phase of each biphasic pulse induced a posterior to anterior current flow in the brain (cf. Hartwigsen et al., 2016, 2010b). Stimulation intensity was set to 90% of a participant's individual resting motor threshold (RMT; cf. Hartwigsen et al., 2015b, 2010a, 2010b). RMT was defined as the lowest intensity needed to cause over 5 motor evoked potentials (MEPs) of size 50 μ V or greater in the relaxed target muscle when stimulating the hand region of M1 10 times. It was determined before the first experimental session by applying single-pulse TMS to left M1 and measuring MEPs in the relaxed first dorsal interosseous muscle of the right hand. To compensate for the depth of the PT-target (mean distance from scalp = 33.52 mm, SD = 2.43 mm), the intensity for PT-stimulation was adjusted accordingly. The following formula was used, adapting the formula by Stokes et al. (2005):

$$\text{PT-Intensity (stimulator output)} = 90\% \text{ RMT} + 3 \cdot (D_{\text{PT}} - D_{\text{M1}})$$

where D_{PT} and D_{M1} correspond to the distance between the subject's scalp and the target in the PT or M1, respectively. Mean coordinates for M1 (MNI: x, y, z = -37 -21 58 mm) from the meta-analysis by Mayka et al. (2006) were used for individual distance correction. The distance correction was applied to 90% RMT (instead of 100% RMT) to avoid unpleasantly

high stimulation intensities. If individual stimulation intensity was too uncomfortable for the subject, it was gradually lowered to the highest intensity still comfortable. The intensity for pIFG-stimulation was not adjusted for distance since the pIFG-target lay very close to the scalp (mean distance = 18.79 mm, SD = 2.20). Our rTMS-protocol followed the published safety guidelines (Rossi et al., 2009).

2.5 Data Analysis

2.5.1 Drift Diffusion Model

Response times (RTs) and accuracy for comprehension questions were analyzed with a drift diffusion model (DDM; Ratcliff, 1978). A DDM reflects the underlying cognitive processes that contribute to a particular response distribution by exploiting the behavioral variation across correct and incorrect trials (Ratcliff, 2014). Unlike average measures of response speed or response accuracy, a DDM thus provides a more fine-grained decomposition of the various cognitive sub-processes that contribute to a decision (Hartwigsen et al., 2015a; Voss et al., 2013), effectively factoring out potential speed–accuracy tradeoffs (Ratcliff et al., 2016). The DDM assumes that during binary decision processes, the subject accumulates evidence for a certain decision from a stimulus, beginning at a starting point (z), until a decision boundary is reached (Figure 3A). In the present study, the decision boundaries corresponded to the success values, whereby the upper boundary (at a) represented correct responses, while the lower boundary (at 0) represented errors. Note that the boundary width (a) determines the amount of evidence that must be accumulated until a decision is reached and thus represents different speed–accuracy settings. The accumulator’s behavior follows a (Wiener) diffusion process, which consists of a systematic influence (towards the correct decision), and a random influence (Gaussian noise) (Voss and Voss, 2007). Because the decision boundaries in our study represented correct and incorrect responses, we assumed that subjects should not be biased towards either correct or incorrect decisions at the start of the trial and thus fixed the

starting point z to $a/2$. The non-decision time parameter (t_0) represents extra-decisional parts of RT (e.g., time for stimulus encoding and response execution). Finally, the drift rate parameter (ν) corresponds to the average rate of evidence accumulation and is determined by the signal-to-noise ratio (Ratcliff et al., 2016). As TMS adds task-unrelated activity to the task-related signal of the stimulated brain region, effectively lowering its signal-to-noise ratio (Siebner et al., 2009), the drift rate was assumed to represent the key parameter influenced by TMS in our study (cf. Georgiev et al., 2016; Hartwigsen et al., 2015a; Philiastides et al., 2011; Soto et al., 2012). Thus, ν was estimated for each experimental condition separately (using 32 trials). All other DDM parameters were estimated for each TMS session separately (using 256 trials). When all parameters are set, the DDM predicts the RT distributions for both available decisions (Voss and Voss, 2007). The parameters are estimated such that the predicted RT distributions optimally fit the empirical RT distributions. We used the freely-available program *fast-dm* (version 30.2; Voss and Voss, 2007; <http://www.psychologie.uni-heidelberg.de/ae/meth/fast-dm/>) to estimate the DDM parameters. The fit of the predicted and empirical RT distributions was optimized using the Maximum Likelihood approach implemented in *fast-dm* (Voss et al., 2013). This method is recommended for small sample sizes, as in the present study, but it can be sensitive to outliers; for this reason, we excluded all trials in which RT deviated more than or equal to 3 SDs from the median RT of the respective experimental run. After all parameters of the DDM had been estimated, the drift rate data was analyzed further. All statistical analyses were performed using *SPSS* (version 23.0; SPSS Inc., Chicago, IL, USA) and *Matlab* (version 9.0/2016a).

Figure 3 here (Single column).

2.5.2 Drift Rates during Sham

We expected differences in drift rates between the different conditions already under ineffective sham-stimulation because numerous behavioral studies have demonstrated a

performance decline for object– versus subject-first sentences (Clifton et al., 1984; Friederici et al., 2006; King and Just, 1991), and for long– versus short-distance sentences (Babyonyshev and Gibson, 1999; Cowper, 1976; Gibson, 2000; Grodner and Gibson, 2005).

Therefore, a first analysis was restricted to the sham-conditions. These data were analyzed with a three-way repeated-measures ANOVA including the factors TMS-TIME (early, late), ORDER (subject-first, object-first), and DISTANCE (short, long).

In a second step, the data from the effective rTMS sessions were normalized to sham to factor out any differences between conditions unrelated to effective stimulation. Specifically, differences in drift rate were calculated between each condition under effective stimulation (pIFG, PT) and their sham-equivalents.

2.5.3 Sham-normalized Drift Rates (pIFG, PT)

The sham-normalized drift rates were analyzed using a four-way repeated measures ANOVA with the factors TMS-SITE (pIFG, PT), TMS-TIME (early, late), ORDER (subject-first, object-first), and DISTANCE (short, long). Significant interactions were further explored using step-down analyses and post-hoc paired t-tests. The significance-level (α) was set to 0.05. *P*-values were corrected for multiple comparisons using the Holm-Bonferroni method (Holm, 1979).

3 Results

The influences of task conditions on the mean drift rate across participants during (ineffective) sham-stimulation are shown in Figure 3B. A repeated-measures ANOVA over the sham drift rates yielded main effects of ORDER ($F_{1,23} = 4.791$; $p = 0.039$) and DISTANCE ($F_{1,23} = 6.765$; $p = 0.016$), with object-first sentences leading to lower drift rates than subject-first sentences, and long-distance sentences causing lower drift rates than short-distance sentences. These effects did not interact with TMS-TIME.

To investigate the disruptive effects of rTMS over pIFG or PT on sentence comprehension, an ANOVA on the sham-normalized drift rates was performed. This analysis revealed a three-way interaction between the factors TMS-SITE, ORDER and DISTANCE ($F_{1,23} = 7.24$; $p = 0.013$), independent of TMS-TIME. Separate analyses within the two levels of the DISTANCE factor (long or short; now pooled across TMS-TIME) showed that this three-way interaction was driven by a TMS-SITE x ORDER interaction for long-distance sentences ($F_{1,23} = 6.87$; $p = 0.015$; Figure 4), but not short-distance sentences ($F_{1,23} = 0.62$; $p = 0.43$). Specifically, pIFG-stimulation lead to significantly lower sham-normalized drift rates for object–, as compared to subject-first, long-distance sentences ($t_{23} = 2.86$; $p = 0.009$). This effect was driven by a numerical decrease in drift rate for object-first sentences after pIFG TMS, as compared to sham, and an increase for their subject-first counterparts. The same comparison for PT-stimulation was far from significant ($t_{23} = -0.11$; $p = 0.9$). Importantly, a direct comparison of both stimulation sites revealed that the difference in drift rates between object– and subject-first long-distance sentences was significantly stronger for pIFG than PT TMS ($t_{23} = -2.62$; $p = 0.015$).

Moreover, separate analyses of the different levels of the ORDER factor showed a TMS-SITE x DISTANCE interaction for subject-first, but not for object-first, sentences ($F_{1,23} = 6.72$; $p = 0.016$). This occurred as pIFG-stimulation induced higher sham-normalized drift rates for long– than short-distance subject-first sentences ($t_{23} = -2.3$; $p = 0.031$; does not survive a correction for multiple comparisons), while PT-stimulation did not produce the same effect ($t_{23} = 0.784$; $p = 0.44$).

Figure 4 here (1.5 column).

To control for potential learning effects across sessions (i.e., behavioral improvements over time), which might have confounded our results, we performed individual Pearson's linear

correlations for each participant over their mean drift rate in the three experimental sessions. Correlations were not significant in any participant (mean p -value: 0.617, SD: 0.289); and correlation coefficients did not significantly differ from zero ($t_{23} = -0.9802$, $p = 0.34$). These results indicate that the data were not confounded by learning effects.

4 Discussion

In this study, we investigated the functional relevance of the left posterior inferior frontal gyrus (pIFG) and planum temporale (PT) for sentence comprehension. Specifically, we hypothesized that focal disruption of pIFG should selectively interfere with the reordering of arguments (i.e., subject and object) in sentences with atypical argument orders, while rTMS over PT should only affect the storage of arguments in sentences with a long argument–verb distance. To this end, we employed a drift diffusion model that is known to be sensitive to TMS-induced changes in behavioral performance. Our main finding supports the first hypothesis, as we found that rTMS over pIFG, but not over PT, significantly increased the performance decline for object–, as compared to subject-first, sentences. Notably, this effect was only observed on long-distance sentences and driven by a numerical decrease in task performance (i.e., impairment) for object-first sentences, and a relative increase in performance (i.e., facilitation) for their subject-first counterparts.

These findings strongly suggest that left pIFG is crucially involved in reordering, at least during the processing of long-distance sentences. Importantly, the use of TMS allows us to draw causal inferences (Walsh and Cowey, 2000), and thus substantially extend previous neuroimaging studies that showed a correlation between reordering demands (atypical vs. typical argument orders) and left pIFG activation (Ben-Shachar et al., 2003; Friederici et al., 2006; Kim et al., 2009). In other words, our findings demonstrate that pIFG activation for reordering is not just incidental to task performance, but that left pIFG is indeed necessary for reordering (in long-distance sentences).

A previous rTMS study by Lauro et al. (2010) corroborates our results. These authors found rTMS over left pIFG to selectively decrease performance on syntactically complex sentences (containing relative clauses), but not on simple sentences. Note, however, that their experimental paradigm did not separate syntactic complexity from storage demands. In contrast, by independently manipulating argument order and argument–verb distance, we were able to disentangle syntactic complexity (i.e., reordering) from storage. Together, the results of both studies indicate that left pIFG causally supports the processing of syntactically complex sentences (e.g., sentences with atypical argument orders, or sentences containing relative clauses).

Why did rTMS over pIFG disrupt reordering selectively on long-distance sentences? One possibility is that pIFG rTMS concomitantly stimulated a region at the border of left anterior IFG and inferior frontal sulcus that is associated with a syntactic working memory system (Makuuchi et al., 2013, 2009). This is plausible due to the spatial resolution of TMS, and potential current spread (Pascual-Leone et al., 1999). Syntactic working memory is dedicated to the storage of syntactically dependent elements (e.g., arguments) in syntactically complex sentences only (e.g., object–, but not subject-first, sentences; cf. Makuuchi et al., 2013; see Makuuchi et al., 2009 for corresponding data on embedded sentences). Consequently, in our study, a disruption of both reordering and syntactic working memory processes would have caused the most severe impairment on object-first long-distance sentences—the exact pattern we observed.

An alternative explanation is task difficulty, because long-distance sentences are generally harder to process than short-distance sentences (see Figure 3B) and difficult experimental conditions are more sensitive to a disruption by TMS: As the relative signal-to-noise ratio was already the lowest without stimulation in these conditions, TMS should have a higher potential of decreasing the ratio to the critical point where it becomes difficult to separate signal from noise, resulting in a disruption of behavioral performance (Siebner et al.,

2009). In the easier conditions, the signal-to-noise ratio might have been high enough to compensate for the disruptive TMS effect and thereby prevent a behavioral impairment (cf. Hartwigsen et al., 2015b).

At first glance, a third possible explanation seems to be that left pIFG might not only contribute to reordering, but also to articulatory rehearsal of verbal working memory content (together with adjacent ventral premotor cortex; Awh et al., 1996; Paulesu et al., 1993; Petrides et al., 1993), which could be crucial for the processing of long-distance sentences. If this were true, then TMS over pIFG would have disrupted both reordering and rehearsal, leading to the strongest impairment on object-first long-distance sentences (cf. Meyer et al., 2014). We believe that this explanation is unlikely for the following reasons: If rehearsal were involved in the processing of long-distance sentences and had indeed been disrupted by pIFG rTMS, then we would have expected a general performance decline for long- vs. short-distance sentences across both order conditions. However, on the contrary, performance even tended to *increase* for long-, as compared to short-distance, subject-first sentences. These results strongly speak against the idea that rehearsal processes were affected.

Note that the role of left pIFG may extend beyond reordering in sentence comprehension to hierarchical sequence processing in other domains. Numerous studies have demonstrated that the pIFG is engaged in the processing of various other types of hierarchically-structured sequences, including sequences of visual symbols (Bahlmann et al., 2009; Tettamanti et al., 2009), music (Maess et al., 2001), and actions (Clerget et al., 2011; Fazio et al., 2009; Koechlin and Jubault, 2006). For example, in a study by Clerget et al. (2009), rTMS over left pIFG selectively impaired the reordering of hierarchically-organized human actions, but not of non-biological events. A different study found TMS over left pIFG to disrupt the processing of a hierarchically-structured sequence of digits (Alamia et al., 2016). Together with our findings, these results suggest that the left pIFG crucially

contributes to the processing of hierarchically-organized sequences (cf. Fadiga et al., 2009; Kemmerer, 2012; Nishitani et al., 2005).

Based on prior psycholinguistic results (cf. Nicol and Swinney, 1989), we initially expected that pIFG rTMS should only affect reordering at the late stimulation time point, when applied with verb onset. However, the disruptive TMS effect occurred across both early and late stimulation. During the long-distance conditions, early TMS was applied with argument onset, when the arguments were encoded in working memory. In contrast, late TMS was applied on the main verb, when arguments and verb were linked. The fact that pIFG-disruption caused an order effect at both time points indicates that this region is crucially involved in reordering both during argument encoding and argument–verb linking. This suggests that the pIFG is engaged in the reordering of arguments into the typical order as soon as they become available (cf. Bornkessel and Schleewsky, 2006; Bornkessel-Schleewsky et al., 2009), but is recruited again when the argument order in working memory has to be matched to the order of argument–verb linking (i.e., the typical order), to perform reordering in case of a mismatch (cf. Meyer et al., 2012b; Nicol and Swinney, 1989). These findings are in line with the proposal that arguments are interpreted incrementally, both independent of and in relation to the verb (Bornkessel and Schleewsky, 2006).

In general, the observed dichotomy of task-specific impairment for object-first long-distance sentences and slight facilitation for their subject-first counterparts converges with the findings from a previous study by Walsh et al. (1998). In that study, TMS over V5/MT impaired performance on a visual search task when motion was relevant to the task and facilitated performance when motion was irrelevant to the task. The reported impairment demonstrates a causal contribution of V5/MT to the processing of visual motion. The authors argued that facilitation occurred since different regions compete for processing resources; eliminating a task-irrelevant region (here: a visual motion area in a non-motion task) from this competition may thus improve performance. This explanation is commonly used to explain

“paradoxical” facilitation effects with disruptive TMS protocols in the study of cognition (Hartwigsen et al., 2015a). We propose that a similar effect occurred in the present study because left pIFG is causally involved in reordering: Reordering is relevant for the processing of object-first sentences, but irrelevant for the processing of subject-first sentences. Hence, a TMS-induced perturbation of the pIFG during object-first sentences should impair performance, but facilitate performance during subject-first sentences. This is exactly what we observed on long-distance sentences.

This explanation is further supported by the activation pattern in a previous fMRI study by Meyer et al. (2012a). In that study, object-first sentences apparently increased task-related activity in left pIFG, whereas their subject-first counterparts showed *deactivation* of this region. Note that these effects were the strongest for long-distance sentences, for which the facilitation-and-impairment effect was found in the present study. Together, the findings of the previous and the present study provide evidence for a selective role of left pIFG in the processing of object-first, but not of subject-first, sentences.

In contrast to our second hypothesis that rTMS over PT should disrupt argument storage, PT TMS did not interfere with storage. This is in disagreement with the previously reported task-specific activation of this region for storage (Meyer et al., 2012a). Several possible explanations might account for the absence of any disruptive effect for PT TMS. First, storage may not rely on the PT, at least not exclusively. Across previous neuroimaging studies, activations for storage of verbal material were widely distributed across the left temporo-parietal cortex (Kim et al., 2002; Novais-Santos et al., 2007; Owen et al., 2005; Smith and Jonides, 1998). Some of these studies even found spatially separated sub-activation-peaks for storage in the same experiment (e.g., Buchsbaum et al., 2001; Meyer et al., 2012a). This large distribution of activations may reflect widely distributed working memory representations. In that case, focal stimulation of PT may not have been sufficient to disturb these

representations, or might have been compensated for by other regions (cf. Hartwigsen et al., 2016). Alternatively, the wide spread of activations may reflect several different processes engaged by an increased argument–verb distance. Indeed, in the previous fMRI study (Meyer et al., 2012a), the authors proposed that in addition to storage, their distance manipulation might have exacerbated working memory retrieval (cf. Meyer et al., 2012b). If this was true, then PT-stimulation may have affected merely one sub-process associated with an increased argument–verb distance, which was not strong enough to cause an observable behavioral impairment.

Another potential reason why no PT-effect was observed is that the storage-relevant PT-region might have lain too deep within the cortex to be stimulated by rTMS: The mean distance between the PT-target and the scalp was 33.52 mm, whereas the pIFG-target lay much closer to the scalp (mean distance: 18.79 mm). We attempted to account for this difference by correcting the intensity for PT TMS for the scalp-to-cortex distance; however, this might not have been sufficient. Notably, the magnetic field strength decreases rapidly with increasing distance from the coil: At a distance of 4 cm from the coil, only about 30% of the intensity strength at the surface is left (Siebner et al., 2009).

It is important to consider whether any confounding (i.e., TMS-unrelated) factors lead to the observed effects in our study. Firstly, the data were not influenced by learning effects: Several correlation analyses on performance changes across the three experimental sessions did not reveal any significant results. Secondly, we are confident that our results were not driven by potential speed–accuracy tradeoff effects: Individual speed–accuracy settings were accounted for by the boundary width parameter (a) of the drift diffusion model, and were thus excluded from the drift rate data. Finally, another potential confound is that ineffective sham-stimulation does not produce the somatosensory stimulus on the scalp that effective TMS produces. This raises the concern that any effects of effective TMS could be related to the

unpleasantness of effective stimulation. However, this possibility is rather unlikely. First, the observed effects were anatomically specific as we only found effects for pIFG TMS, but not for PT-stimulation. Second, the effects were task-specific as pIFG TMS impaired performance on object-first long-distance sentences only, and even slightly *improved* performance on their subject-first counterparts. It is thus extremely unlikely that the observed effects were merely due to the unspecific side effects of pIFG-stimulation.

Note that besides the critical role of the left pIFG demonstrated here, other regions might also contribute to the processing of syntactically complex sentences. In a recent meta-analysis of neuroimaging studies on complex sentence processing by Meyer and Friederici (2015), left pIFG was the region with the highest activation likelihood, underscoring its outstanding role in complex sentence processing. Other regions that showed significant activation overlap across studies, although less consistently, included parts of the left dorsolateral prefrontal cortex and posterior temporal cortex. Future studies should thus investigate the functional relevance of these regions for complex sentence processing.

In conclusion, our findings provide evidence for a causal contribution of the left pIFG to argument reordering during the processing of object-first sentences with a long argument–verb distance. This is the first study demonstrating a causal role of left pIFG in the processing of syntactically complex sentences that systematically separated syntactic complexity (here: atypical argument order) from working memory demands. Our results might help resolve the long-standing debate about the role of left pIFG in language comprehension.

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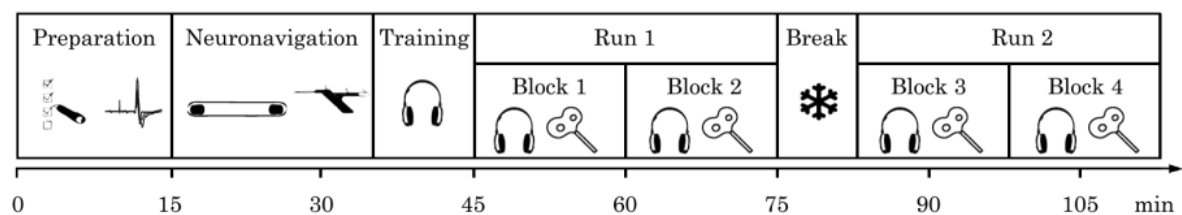
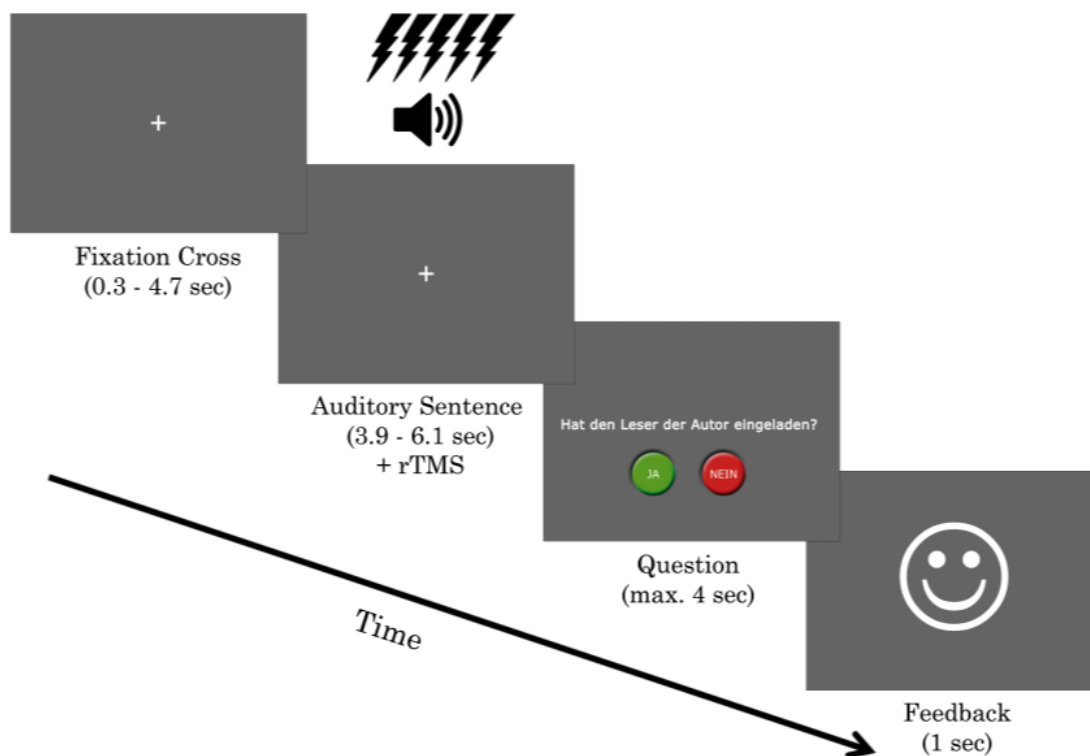
Figure 1: Experimental procedure. (A) Timeline of the experiment (one session). After preparation and neuronavigation, subjects were trained with 10 demo-stimuli. Subsequently, they performed two experimental runs of 128 trials, which were split into two blocks of 64 trials each. (B) Timeline of one experimental trial. A fixation cross was shown on the screen, followed by the presentation of an auditory German sentence, during which rTMS was applied. Afterwards, subjects had to answer a visual comprehension question. Finally, visual feedback was presented.

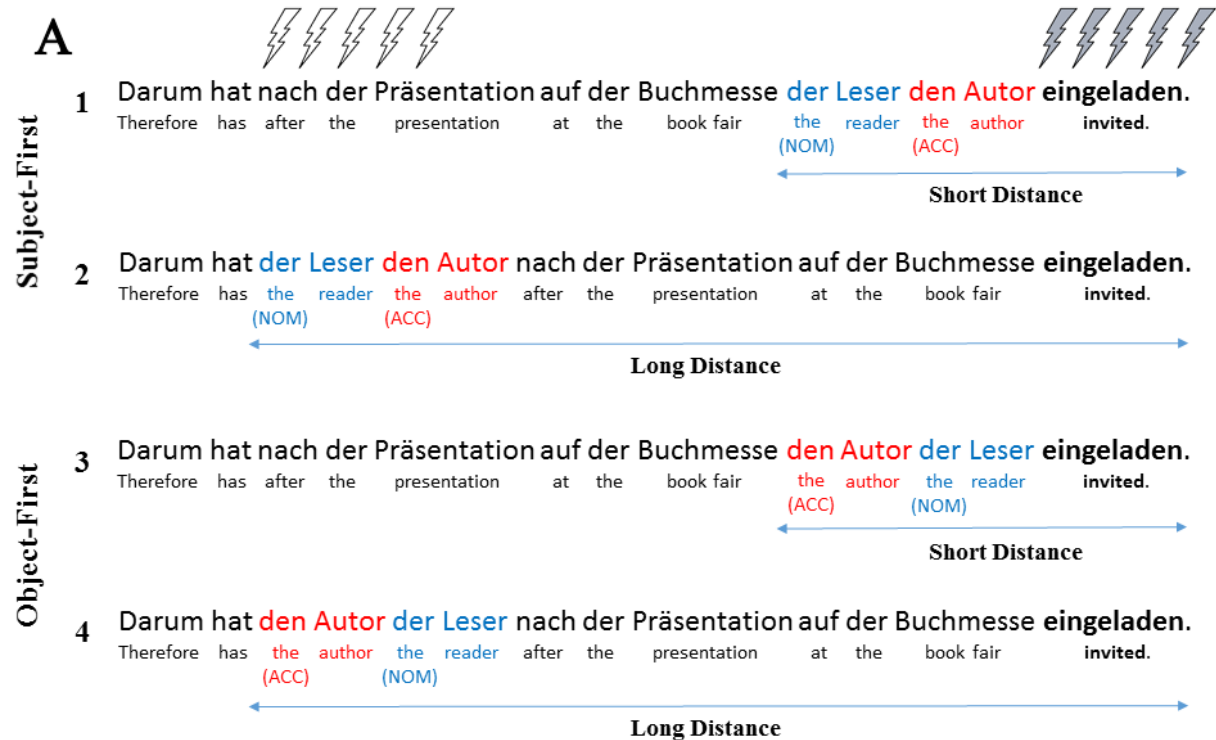
Figure 2: (A) Stimulus material and rTMS application. Subjects (blue) are in nominal case (NOM), objects (red) in accusative case (ACC). The verb is highlighted in bold. All four example sentences translate to: “Therefore, the reader invited the author after the presentation at the book fair”. During sentence presentation, rTMS was applied either early—on the word after the auxiliary verb (white bolts), or late—on the main verb (grey bolts). (B) Types of comprehension questions. Example questions for the sentences in A are depicted, with the respective correct answer given in italics. PP = prepositional phrase. (C) rTMS sites. Coordinates are given in MNI-space. For sham-stimulation, the coil was navigated to the primary motor cortex (M1), and a second coil was placed in a 90° angle above the first coil. Only the second coil was charged to produce a comparable acoustic stimulus without stimulating the brain. pIFG = posterior inferior frontal gyrus; PT = planum temporale.

Figure 3: (A) A schematic illustration of the Drift Diffusion Model (DDM). The subject is assumed to accumulate evidence (represented as a noisy line) at a certain rate (drift rate = v) from a starting point (z) until reaching a decision boundary. The upper boundary (at a) represents correct decisions, while the lower boundary (at 0) represents incorrect decisions.

The two sample paths show different drift rates, with the right path exhibiting a lower ν than the left. Adapted from Wagenmakers et al. (2007). (B) Mean drift rates during sham-stimulation (pooled over TMS-TIME). Object-first sentences lead to lower drift rates than subject-first sentences (main effect of ORDER), while long-distance sentences showed lower drift rates than short-distance sentences (main effect of DISTANCE). Error bars represent standard error of the mean.

Figure 4: Mean drift rates normalized to sham (pooled over TMS-TIME). rTMS over pIFG significantly increased the performance difference between object- and subject-first long-distance sentences. This effect was significantly stronger than the same comparison for PT rTMS. Error bars represent standard error of the mean. n.s.: not significant, *: $p < 0.05$, **: $p < 0.01$.

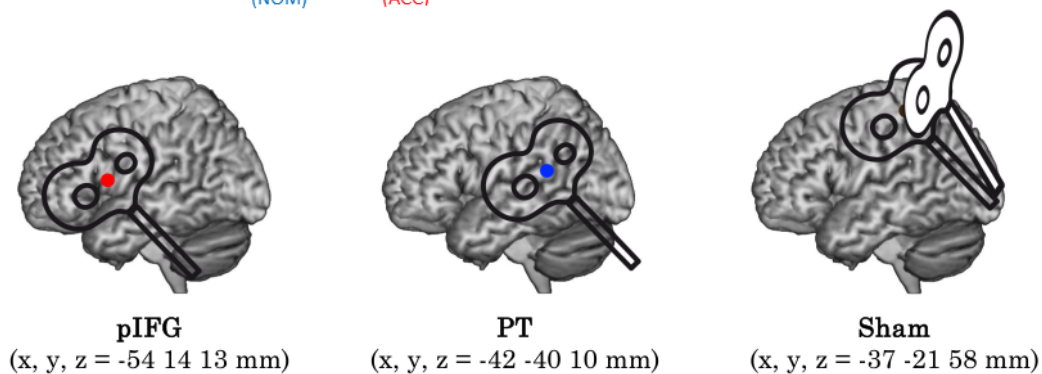
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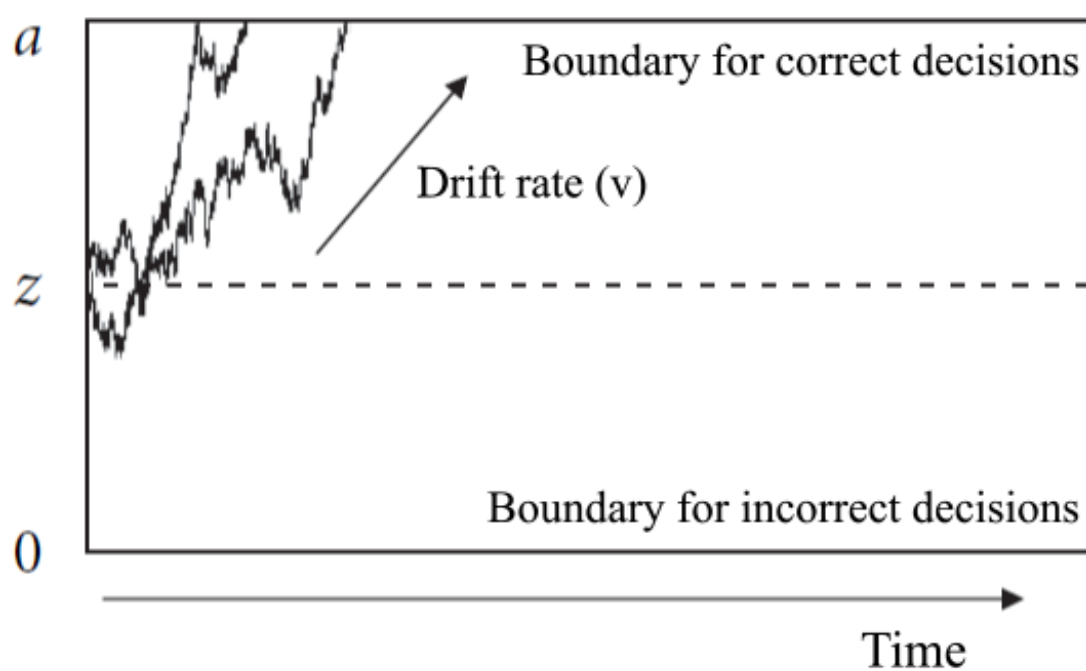
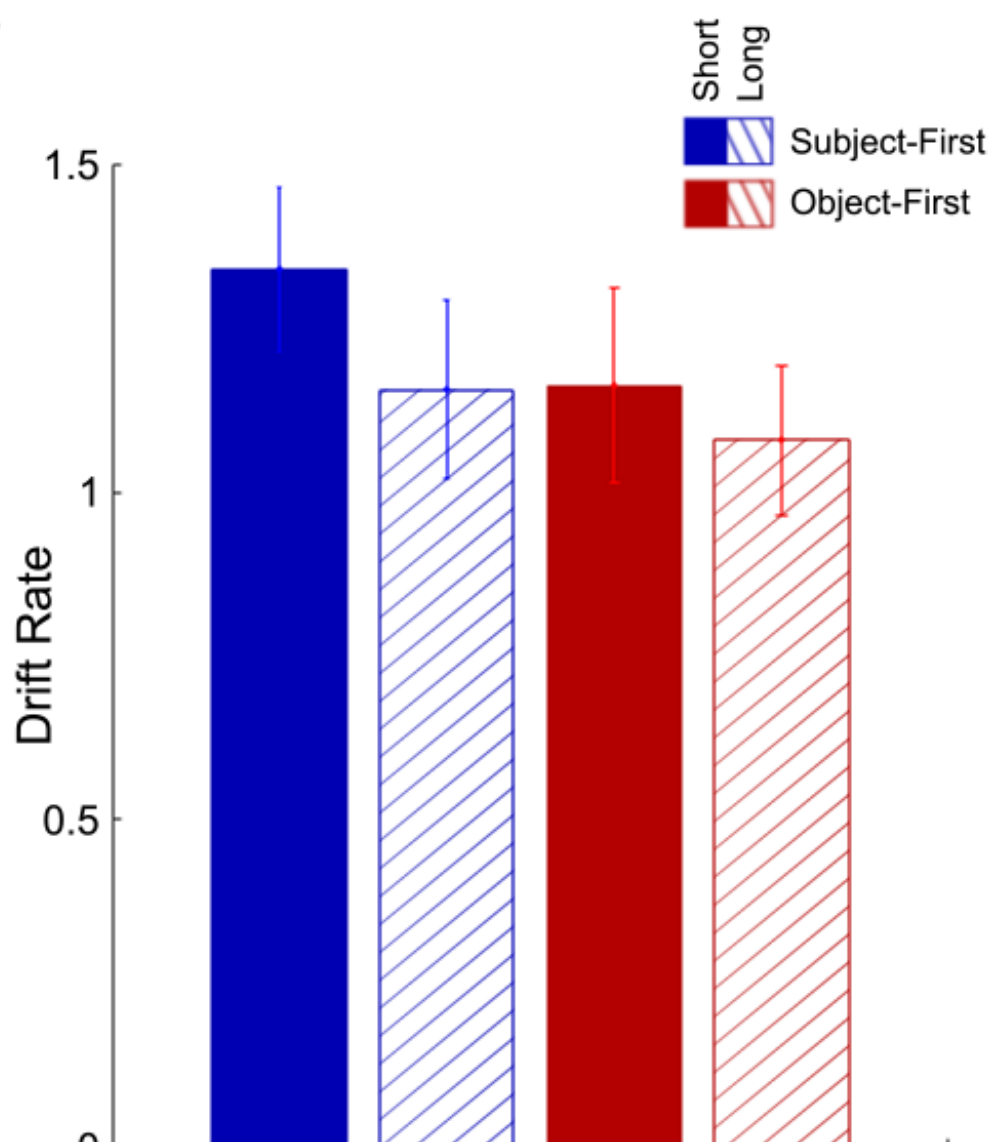


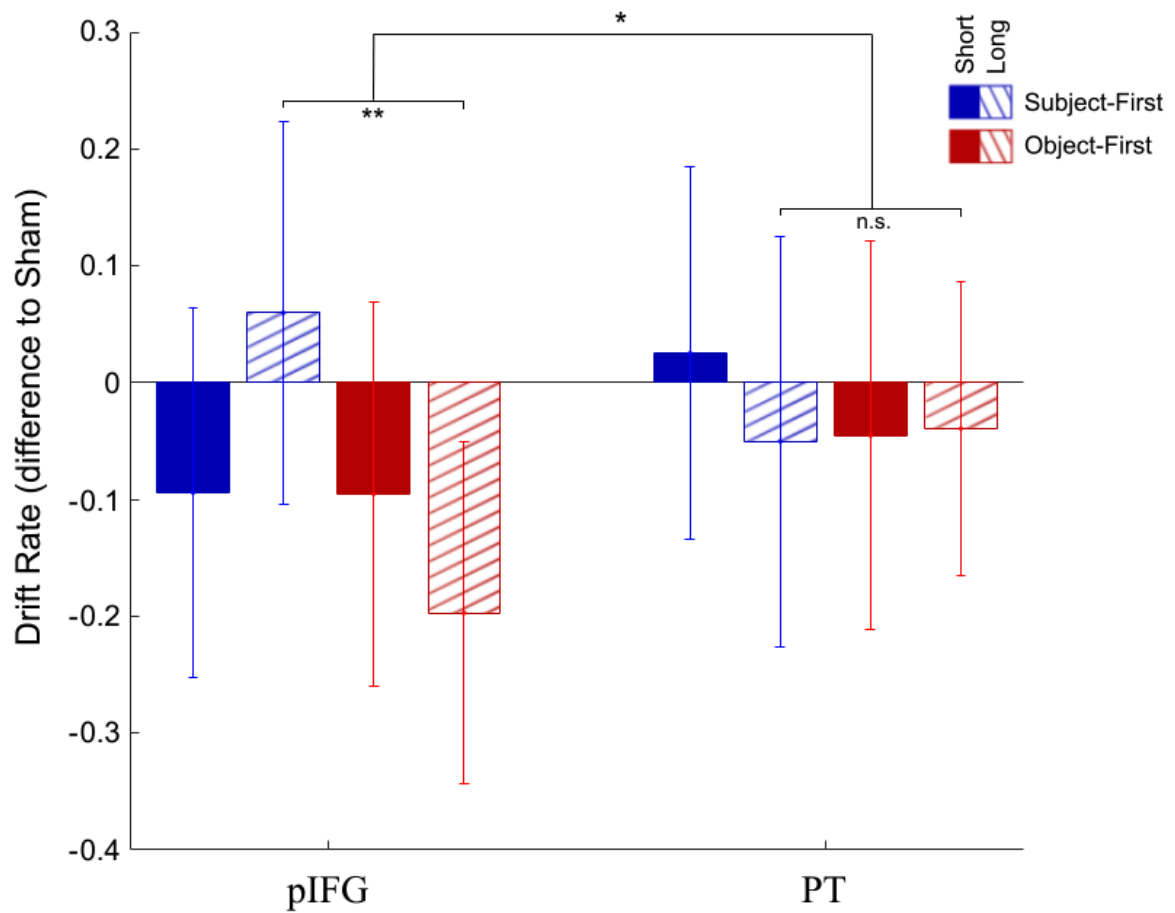
B

- 1 **Subject-First** Hat **der Leser** **den Autor** eingeladen? Yes
Has **the reader** **the author** invited?
(NOM) (ACC)
- 2 **Object-First** Hat **den Leser** **der Autor** eingeladen? No
Has **the reader** **the author** invited?
(ACC) (NOM)
- 3 **PP-Control** Hat **der Leser** **den Autor** auf der Konferenz eingeladen? No
Has **the reader** **the author** at the conference invited?
(NOM) (ACC)

C



A**B**



Highlights

- TMS over left pIFG disrupts argument reordering during sentence processing
- pIFG-TMS increases performance decline for object- vs. subject-first sentences
- pIFG-TMS selectively impairs sentences with a long argument–verb distance
- Left pIFG is necessary for reordering during sentence comprehension