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THE ROLE OF LEFT INFERIOR FRONTAL GYRUS IN MEMORY FOR PREDICTABLE AND UNPREDICTABLE WORDS: AN EVENT RELATED TRANSCRANIAL MAGNETIC STIMULATION STUDY.

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Introduction

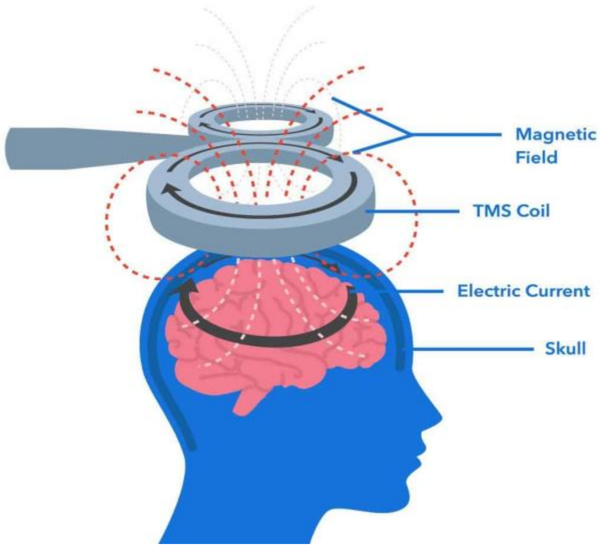
Humans are capable of processing language with remarkable speed and skill. One way that our minds achieve this feat is through drawing on the sentential context to make predictions about upcoming linguistic input (Kuperberg & Jaeger, 2016). For instance, if we were conversing about our coffee preferences, and I were to say that "I like my coffee with cream and…", you will likely predict that you are about to hear me say "sugar" based on prior experiences stored in your long-term memory. However, I could also end up violating your prediction. I may prefer to take my coffee with cream and *honey,* after all.

The speed with which the mind processes both highly-predictable words and prediction violations has been thoroughly investigated through behavioral and neuroimaging techniques. It has been found that when the linguistic input received matches our prediction, word recognition will show facilitated processing. In our aforementioned example, this would be *sugar*. On the other hand, prediction violations (in our context, *honey)* are slower to be recognized and will exhibit hindered processing (Federmeier, Kutas, & Schul, 2010; Payne & Federmeier, 2017).

However, two questions regarding this predictive process in language comprehension require further investigation. The first question is the subsequent fate of these words in long-term memory. There is conflicting evidence on this question in the present literature. Some studies have pointed to a recall advantage for highly-predictable words (Riggs, Wingfield, & Tun, 1993), whereas others point to prediction violations taking on a particular salience in one's memory (Rommers & Federmeier, 2018). A second key question that is not yet fully understood concerns the neural mechanisms that are underlying and facilitating this process. It has been hypothesized that an area of the brain known for speech production, the Left Inferior Frontal Gyrus (LIFG), otherwise known as Broca's Area, is actually being recruited for this important aspect of language comprehension (Pickering & Garrod, 2013). Together, these are the two key questions of the present study.

We utilized a technique that is quite novel to the investigation of language in the brain, transcranial magnetic stimulation (TMS). This is a non-invasive experimental procedure which uses a stimulation coil that has electric wire running through it in a figure-eight configuration. Electrical current runs through the coil and generates a magnetic field when the stimulation is administered. This coil is held flush to the scalp, allowing the magnetic field to penetrate into the brain. This change in the magnetic field induces a secondary electrical current in the brain, causing changes to ongoing neural activity. In this way, it can temporarily disrupt normal neuroprocessing with great focal precision by creating "neural noise," in a sense, to a particular area of the brain (Stewart & Walsh, 2006). A simplified visual diagram of how this process works can be seen in Figure 1.

Figure 1. A simplified visual diagram of a TMS procedure.



In the present study, our two areas of focus were the LIFG in the experimental condition, and its homologue, the Right Inferior Frontal Gyrus (RIFG), for the control condition. The RIFG was chosen as a control site because it is not believed to play any significant role in speech production for those who are left-lateralized for language. This TMS procedure was carried out while participants completed a simple language categorization task, where they were given a semantic category and asked to determine whether or not a subsequent target word was a member of that category.

It was our hope that we would both (1) clarify our understanding of what memory (dis)advantages may exist for words of varying degrees of predictability when the brain is carrying out linguistic functions as it normally would, and that by disrupting normal linguistic functioning through administration of TMS to LIFG and observing the effects on subsequent memory of these words, we would (2) enlighten our understanding of LIFG's potential role in this predictive process. If LIFG does facilitate in the prediction process, we would expect inhibition of this area of the brain through TMS to subsequently level any memory advantages observed when the brain engages in typical language processing.

As an important note, this study is still in its piloting stage. The data presented is therefore qualitative in nature and should be regarded as strictly preliminary.

Methods

Participants

We had nine participants, with a mean age of 25. Participants had to meet several requirements in order to be eligible to participant. They had to be native English speakers with no exposure to another language before the age of three, as early bilingual exposure may influence how the brain is lateralized for language. On a similar note, participants had to also be right-handed, due to a small segment of the left-handed population showing increased bilateral language involvement. To determine handedness, participants were given the Edinburgh Handedness Assessment, which asked them what hand they used for common daily activities. Additional exclusionary criteria included implanted metal, as well as a history of stroke, seizures, psychiatric disorders, epilepsy or brain injuries. This was done to ensure a participant's safety during the TMS procedure. Although TMS has no known effects on prenatal health, pregnancy was also included as an exclusionary criterion as a precaution. Female participants were asked to take a pregnancy test upon arrival.

Materials

One-hundred twenty semantic category cues were used during the experimental procedure, which were adapted from Federmeier, Kutas & Schul (2010). Each category cue was followed by a target word from one of three different sets, grouped by typicality relative to that specific semantic category: a high-typicality word, a low-typicality word, and a semantically incongruent word. Target words were adapted from prior language production research, in which participants were given semantic categories and asked to produce examples of that category, with a word's production frequency subsequently used to conceptualize typicality. In the present study, where we are interested in the construct of predictability, high-typicality words were operationalized as predictable words, and low-typicality words were operationalized as unpredictable words. Incongruent words were words that were outside of the semantic category cue. Examples of category cues and their respective target words are given in Figure 2.

Figure 2. Stimuli examples for category cues and target words for that category cue.

Category Cue	**Predictable Target Word**	**Unpredictable Target Word**	**Incongruent Target Word**
A common color	Yellow	Silver	Tunnel
A kitchen utensil	Spatula	Sponge	Harmony
A non-alcoholic beverage	Tea	Punch	Cart
A kind of snake	Cobra	Anaconda	Academy
A type of condiment	Ketchup	Horseradish	Fraction

Experimental Procedure

Language Categorization Task

The language categorization task was administered through *PsychoPy* experimental software, with stimuli displayed visually on a desktop computer. Participants were presented with a category cue (i.e., "a type of…" or "a kind of…") via Rapid Serial Visual Presentation (RSVP), in which words were displayed on the screen one at a time in intervals of 500ms. The target word was presented 1000ms after the category cue. There were 120 trials in total, with 60 each in the experimental condition (TMS administered to the left hemisphere) and the control condition (TMS administered to the right hemisphere). This study therefore utilized a 2x3 factor, within-subject experimental design, with each participant acting as their own control. The experimental design is summarized in Figure 3.

Figure 3. Summary of the experimental design of the study.

	Predictable Target Word	**Unpredictable Target Word**	**Incongruent Target Word**
Experimental Condition (TMS to LIFG)	20 trials	20 trials	20 trials
Control Condition (TMS to RIFG)	20 trials	20 trials	20 trials

Language items were counterbalanced across condition, stimulation target (LIFG or RIFG), and stimulation order (first block, second block).

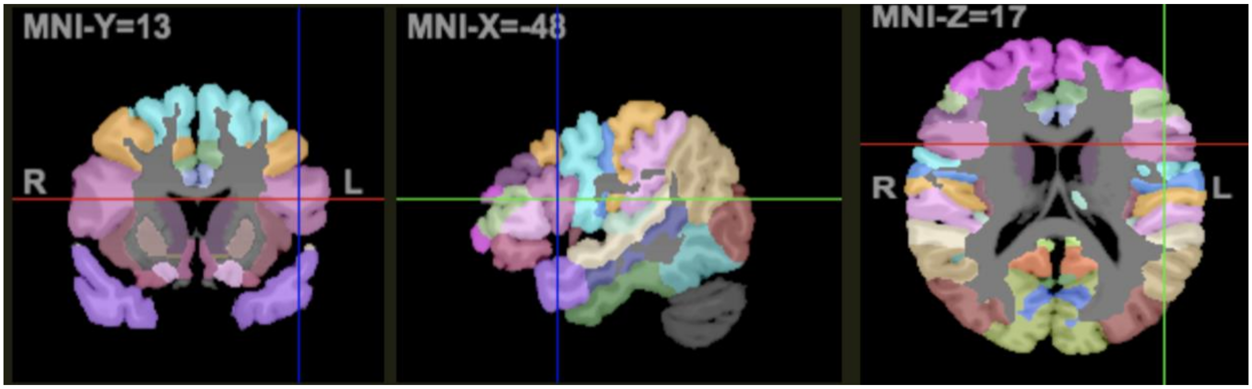
Transcranial Magnetic Stimulation

During the language categorization task, transcranial magnetic stimulation was applied in two separate blocks to either LIFG (experimental condition) and RIFG (control condition). The stimulation was event-related, time-locked to the onset of the category cue. It is at the onset of the category cue where we would expect participants to begin making their predictions for the upcoming target word, thereby disrupting the predictive process in the experimental condition, if indeed LIFG is involved. TMS always occurred in a 5 Hz, 5 pulse train, a stimulation protocol previously found to induce language production errors when administered to LIFG (Tarapore, Findlay, Honma, Mizuiri, Houde, Berger, & Nagarajan, 2013). The language production errors induced through this protocol included instances of anomia, as well as hesitant speech.

Each participant had their TMS stimulation intensity for the experimental procedure individually set, determined by identifying a motor-evoked potential (MEP) threshold. The MEP threshold was the lowest stimulus intensity that elicited a peak-to-peak amplitude of greater than 50 microvolts. The protocol for this was to administer the TMS to the part of the participant's motor cortex responsible for the handknob, starting at a power level of 40%. From there, power levels were either increased or decreased by 1% until a reliable MEP was elicited 50% of the time. If no MEP could be reliably determined, a default power level of 40% was used. Before the start of each block of the language categorization task, the TMS was administered in the 5 Hz, 5 pulse train to the IFG site to be used in that block, and the participant was asked if that stimulation level was comfortable. In cases where the participant verbally identified the stimulation level as uncomfortable, the stimulation level was lowered until a comfortable level for the participant was verbally identified.

Locations for a participant's motor cortex, LIFG and RIFG were determined through the use of the neuro-navigation software *BrainSight*. For this protocol, we began with the ICBM MNI (Montreal Neurological Institute) 152 template, which was created through averaging together MRI scans from 152 participants. We then took samples around the participant's head by using particular landmarks, including the nasion, left preauricular area, and right preauricular area. The software then used these samples to resize the template to better match the participant's head. From there, Brodmann areas were used via the MNI coordinate space, creating accurate targets to which the TMS coil was aligned. Figure 4 shows the location of LIFG (BA-44), the site stimulated in the experimental condition.

Figure 4. Neuro-navigation target of LIFG (BA-44) in the MNI coordinate space. Brodmann areas overlaid in color. See Lacadie, Fulbright, Rajeevan, Constable & Papademtris (2008) for more information.



Recall Task

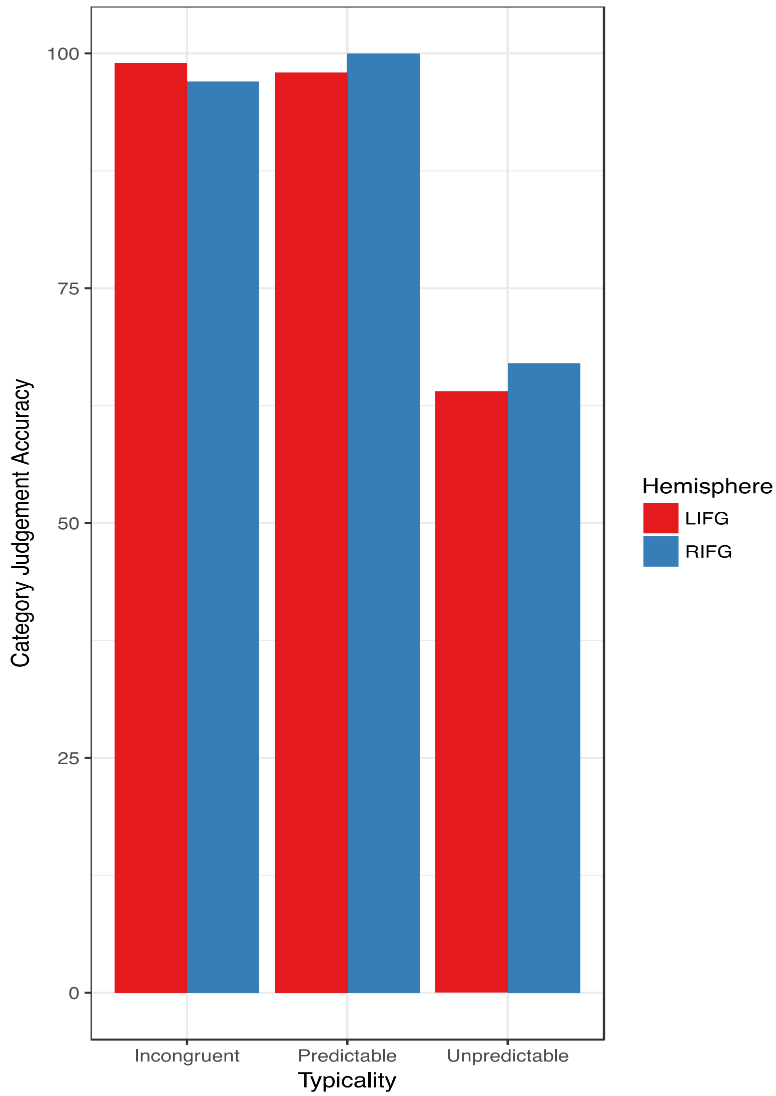
Following completion of the experiment, participants were given a cued-recall task. Participants were presented with a subset of the category cues from the language categorization task, and asked to write which target word was associated with the particular category. Data from the recall task where used to assess how well target words of varying predictability were remembered.

Results

As a reminder, our primary research interests were (1) if there were any differences in how well predictable, unpredictable words and incongruent were remembered, and (2) if inhibition of LIFG through TMS at the precise point of prediction generation led to discernable effects on memory of these words. Due to a small *N*, no inferential statistical analysis was conducted, and the statistics presented here are strictly descriptive in nature.

Data from the recall task was first assessed to determine if TMS interfered with participant's abilities to accurately categorize the target words. Figure 5 shows that participants accurately categorized predictable, unpredictable and incongruent words at comparable rates between the experimental TMS condition and control TMS condition.

Figure 5. Accuracy on category judgments.



The recall data was then assessed to determine how well predictable, unpredictable and incongruent target words were accurately remembered. Figure 6 shows participant's recall accuracy for target words based on typicality between the two conditions. Figure 7 shows the effect of TMS on accuracy in the recall task within our participants between our two hemispheric targets, with target words again grouped by typicality.

Figure 6. Accuracy on the recall task, with recall accuracy on the y-axis and target word typicality on the x-axis.

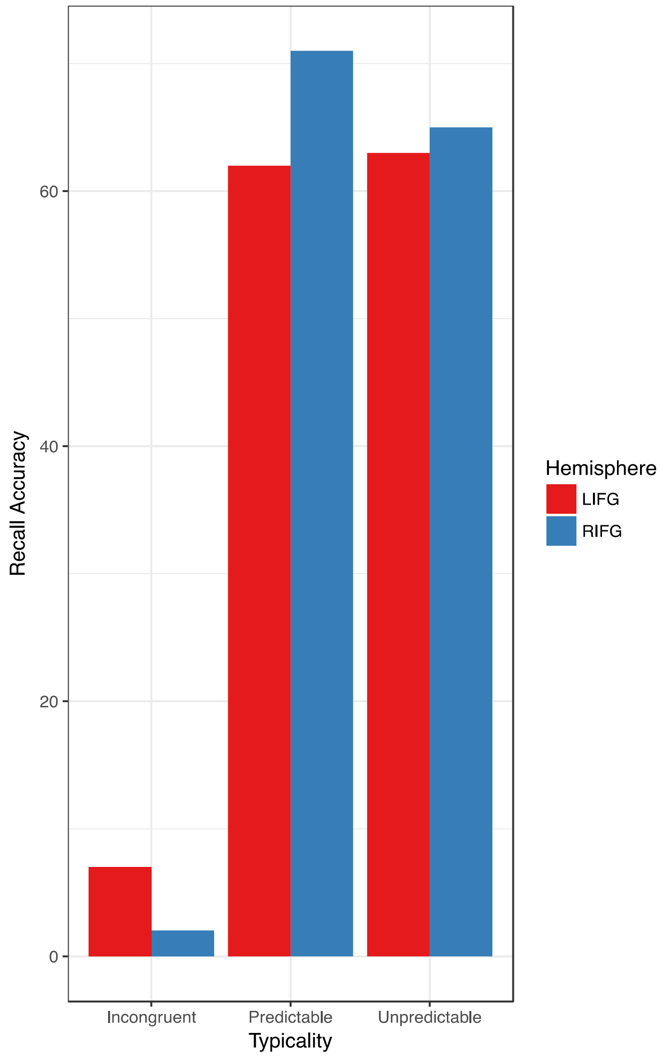
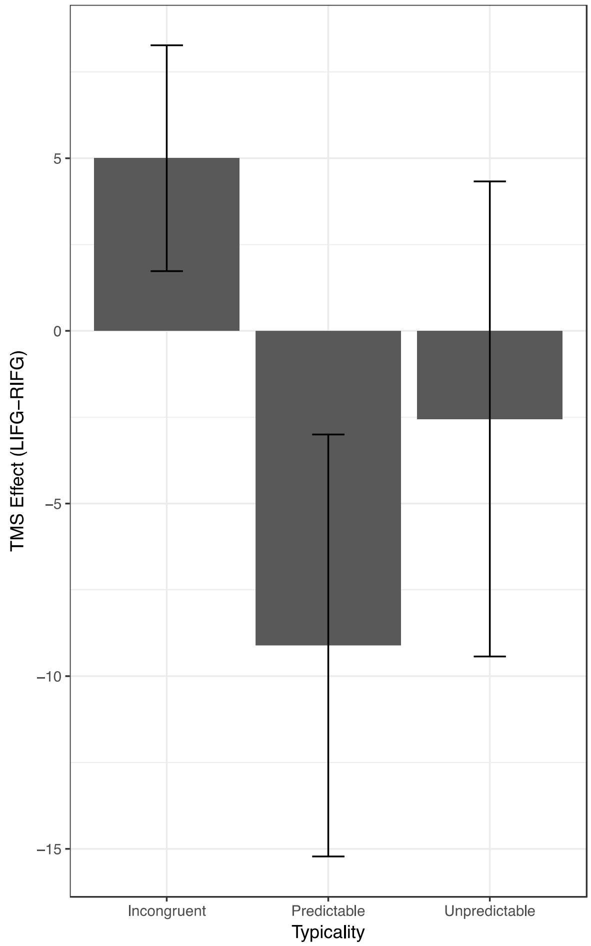


Figure 7. Within-subject differences between the RIFG & LIFG conditions on the recall task, summarized by target word typicality.



Discussion

The research objectives of the present study were to (1) determine the effect of word predictability on its fate in long-term memory, and (2) if inhibition of LIFG during a language categorization task at the point of prediction generation has effects on a participant's subsequent memory of words, thereby implicating it as facilitator in the prediction process. Our results shed some light on both of these questions, but it is again important to note that the data presented here, although promising, is strictly preliminary. This study is ongoing, and participants are still being actively recruited.

From the recall accuracy data, we see a long-term memory advantage for highly-predictable target words in the control condition, where TMS was administered to RIFG. Recall that RIFG is not believed to play a significant role in language-related behavior. Therefore, the accuracy data here paints for us a picture of how well predictable and unpredictable words are retained in long-term memory when the brain is functioning normally for language, with improved recall for the former.

Interestingly, the recall accuracy data shows that this long-term memory advantage for highly-predictable target words was effectively leveled in the experimental condition, with no observable differences in recall accuracy between the two types of semantically congruent words. It was in this condition that the TMS was applied to LIFG at a stimulation level previously shown to impair its normal functioning for language production. Importantly, the TMS was administered at the category cue in the language task, the exact point when we would expect participants to be recruiting the language production system to generate predictions for what target words they may subsequently see. Our results show an interference effect of TMS to LIFG, negatively impacting how well the highly-predictable target words are subsequently remembered. The effect of TMS inhibition of LIFG at the moment of prediction generation points to it being involved in the encoding of (un)predictable words within long-term memory. As accessing long-term memory during language comprehension to make predictions about upcoming linguistic input based on prior experiences, the results here show how LIFG may be recruited to facilitate the predictive process.

Although they were not the primary focus of this study, the exceptionally poor recall of the semantically incongruent target words in both conditions does merit some discussion. One possible reason for this result could be the fact that recall here would need to necessarily rely entirely on associative memory. Arbitrary associations between category cues and target words would need to be mapped on to each other for the first time during a trial, and then subsequently recalled after having had only one such exposure to the association. There would be no advantage of semantic cuing for the incongruent words, in which even just presenting a participant with a semantic category brings online a set of potential category members for them to access.

These preliminary results have important implications, both for the study of the specific linguistic role of LIFG, and for the study of language in the brain more broadly. In challenge to classical localizationist models of language, which posit strict divisions of labor between areas of the brain for production and comprehension, our data point to LIFG playing an important role in language comprehension processes. This is due to how crucial the generation of predictions for upcoming linguistic input is for our abilities to comprehend language so quickly. Perhaps even more excitingly, these results demonstrate the utility of event-related TMS to investigate the causal neural mechanisms of specific language functions not offered by other neuroimaging techniques, such as EEG and fMRI. TMS' unique ability to temporarily disrupt normal language processing with high spatial and temporal resolution can allow us to observe the specific effects of inducing inhibition of a particular area of the brain, therefore shedding a clearer light on that area's role in typical cognition.

It is again important to note that the data presented here is strictly preliminary. This study is ongoing, and participants are still being actively recruited.

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