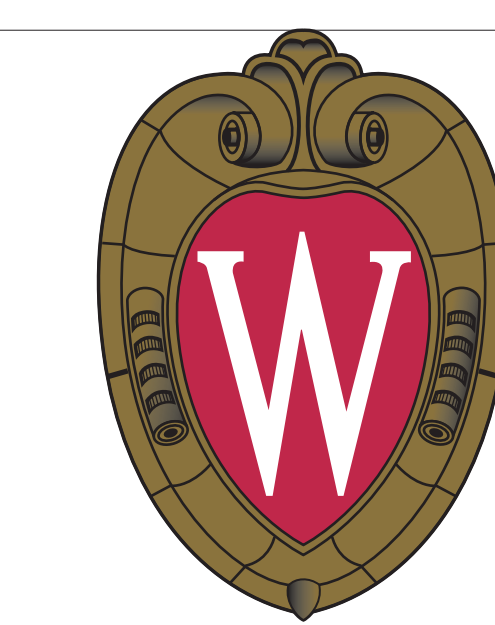


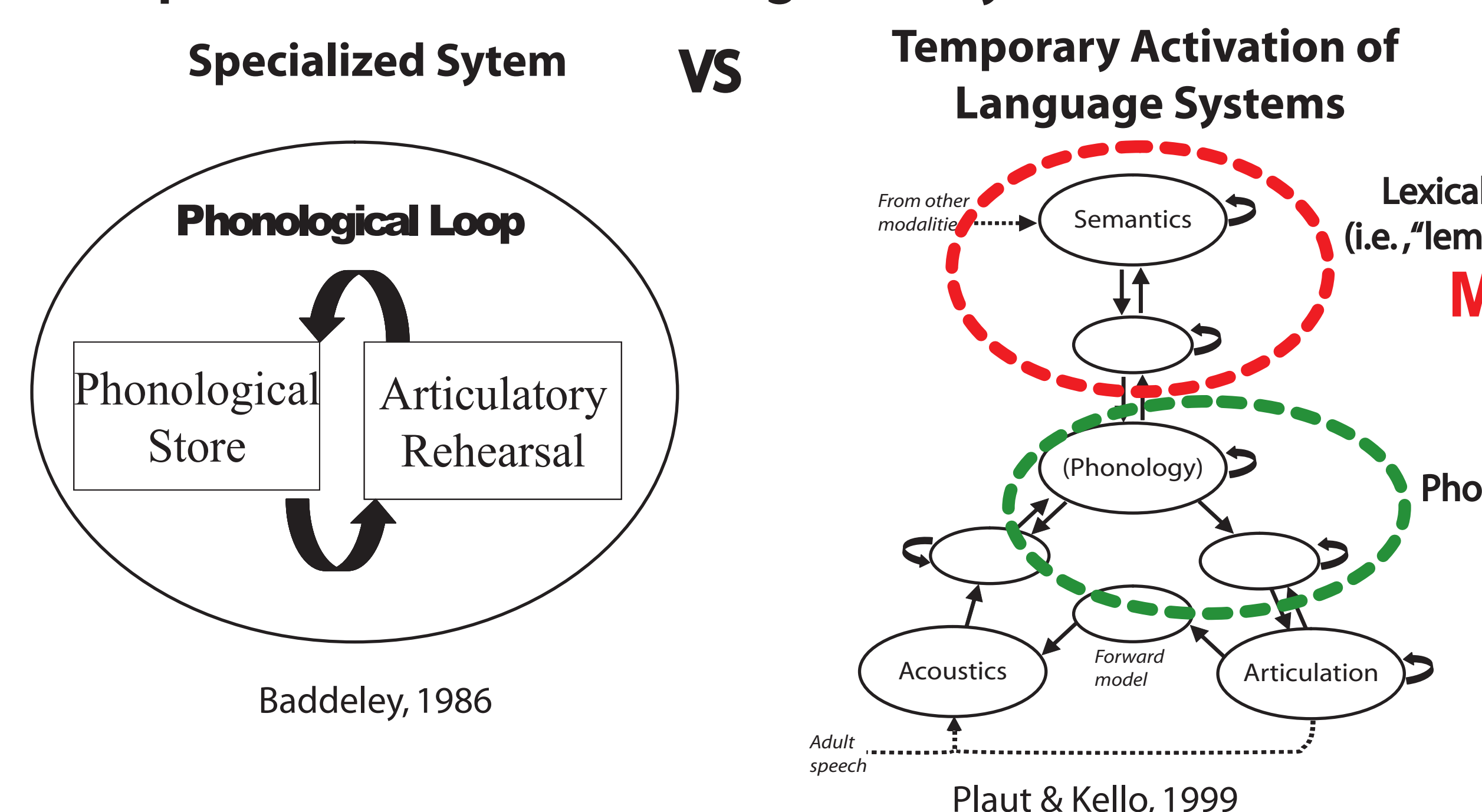
Verbal Working Memory Maintenance Depends on Language Production Systems: A Functionally Guided rTMS Investigation



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Introduction

Perspectives on Verbal Working Memory (WM) Maintenance



Present Study: Testing a Language Production-based Locus to WM Maintenance (Acheson & MacDonald, 2009; Buchsbaum & D'Esposito, 2006)

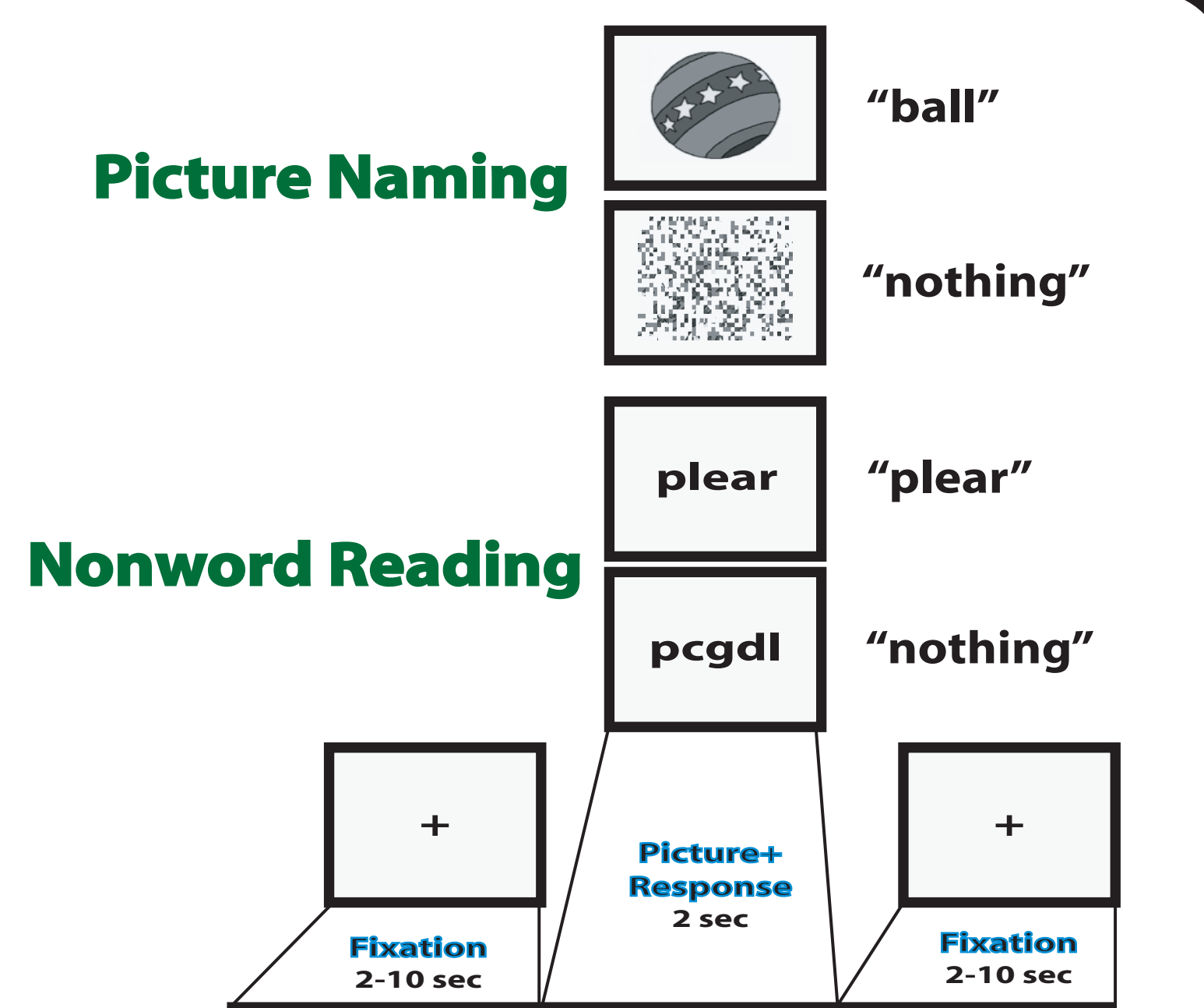
1. Dissociate sub-processes of language production (Indefrey & Levelt, 2004)
2. Target these regions with rTMS as people perform language production and verbal WM tasks
 - Picture Naming
 - Rapid Reading and Delayed Serial Recall of Nonwords

Prediction: Dissociation in the Effect of rTMS on Performance by Region Stimulated

	Picture Naming	Rapid Reading	Delayed Recall
pSTG	-	X	X
MTG	X	-	-

fMRI Procedure

- Design:** Rapid Event-Related, with random stimulus presentation jittered in time
ISIs ranged between 4-12 seconds
- Acquisition:** Whole-brain T1-weighted images (3T GE Signa VH/I)
Anatomical: 256 sagittal slices
256X192 matrix (0.9375 mm X 0.9375 mm X 0.8 mm, no skip)
- Functional:* 30 axial slices
gradient echo, echoplanar sequence (TR=2000ms, TE=50ms)
64X64 matrix (3.75mm X 3.75 mm X 4 mm, no skip)
- Data Analysis:**
BOLD response was modeled using AFNI Gamma functions (GAM)

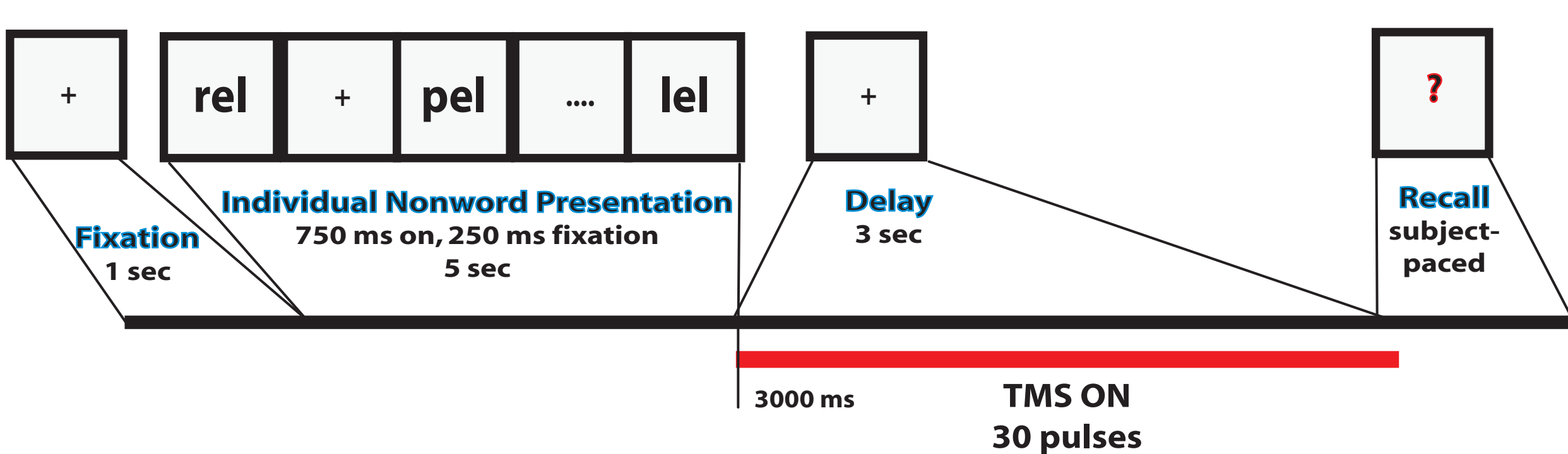


rTMS Procedure

- Picture Naming**
- Participants named color pictures of common objects (Rossion & Pourtis, 2004)
 - rTMS designed to target lexical-semantic access, occurring 100 ms prior through 200 ms after stimulus onset (4 pulses; Indefrey & Levelt, 2004)
 - 80 trials per region

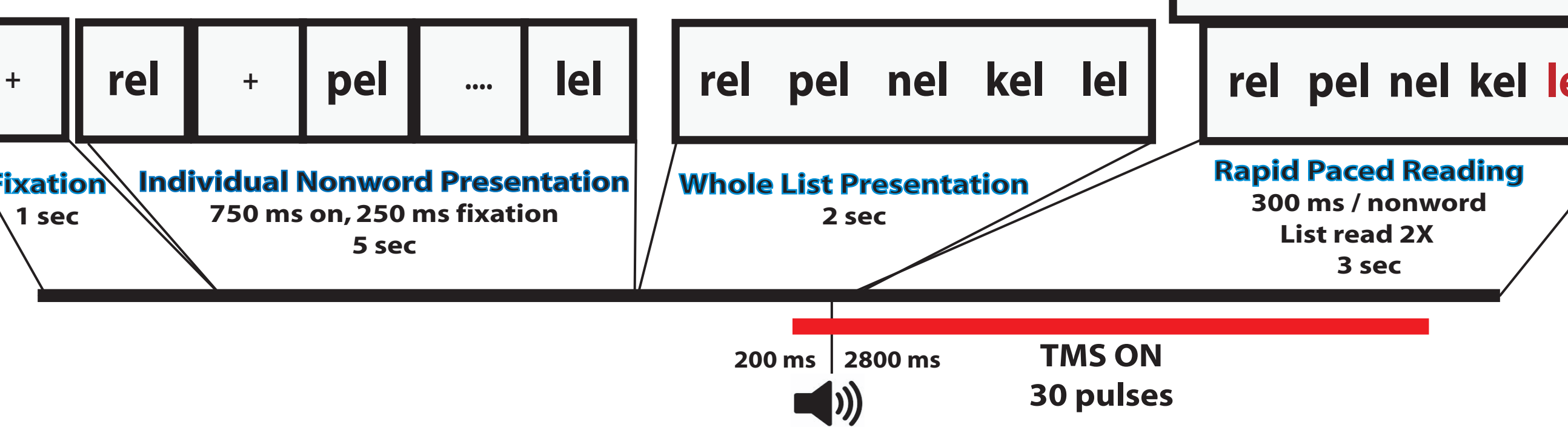
Delayed Serial Recall

- Participants read a list of 5 rhyming nonwords out loud at a rate of 1 nonword/sec followed by a delay of 3 seconds
- rTMS began at the onset of the delay and continued for 3 secs (30 pulses)
- 40 trials per region



Rapid Paced-Reading

- Participants presented with a list of 5 rhyming nonwords one-at-a-time
- Whole list was presented for 2 seconds to allow participants to prepare to speak
- Paced-reading initiated by a tone, read at a rate of 300 ms/nonword; the whole list was read twice
- rTMS occurred for 3 seconds starting 200 ms before paced reading (30 pulses)
- 40 trial per region, half with rTMS



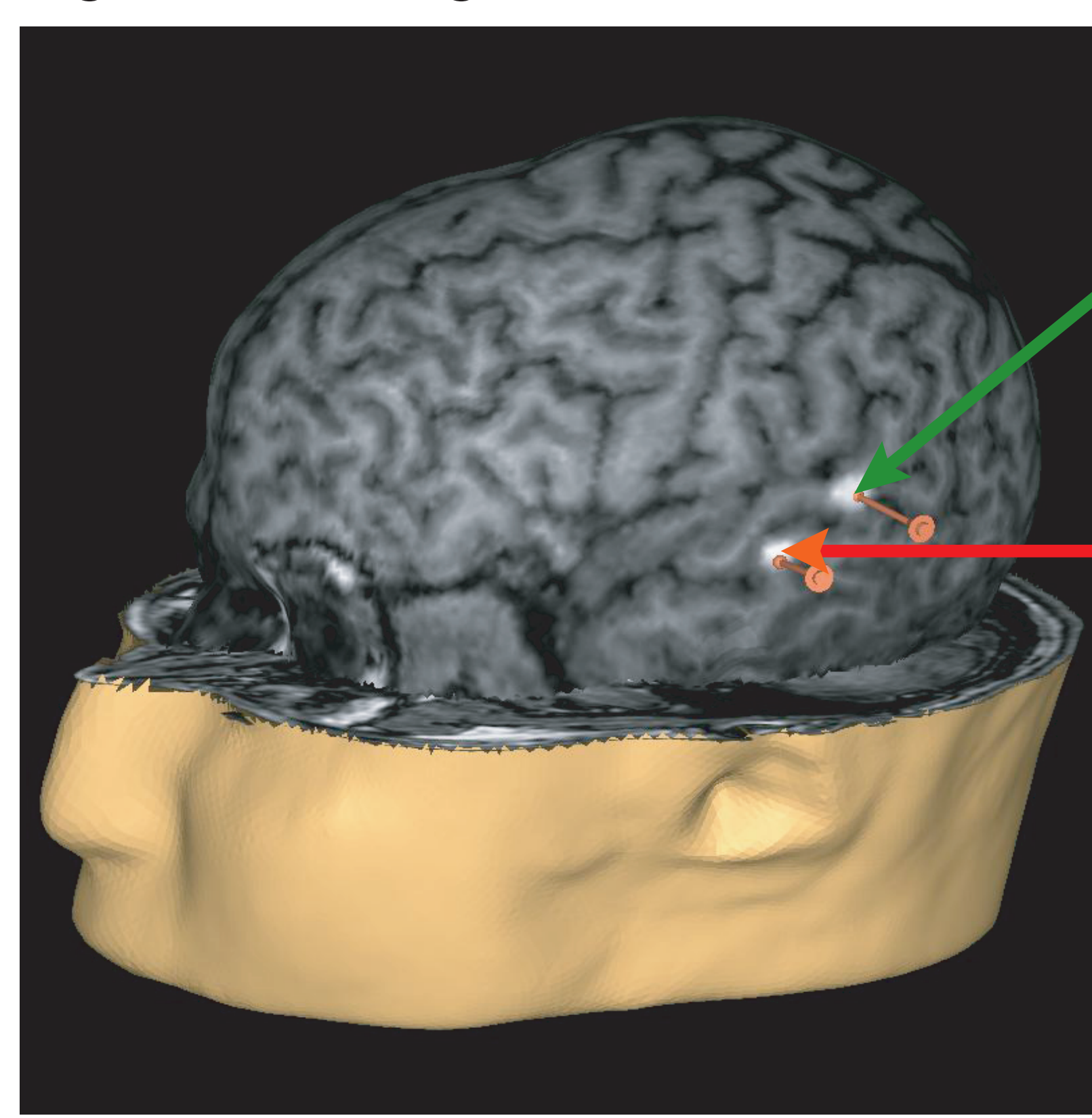
- Each subject's head was coregistered with his/her MRI using eXimia Navigated Brain Stimulation (NBS) frameless stereotaxy navigation system (Nexstim).
- rTMS (10 Hz, 110% MT, -Magstim Standard Rapid, Whitland, UK)
- Stimulation timing varied depending on the task, but occurred randomly on half the trials
- Stimulation intensity was corrected for scalp-to-cortex distance (Stokes et al., 2005).
- Location of targets determined by individual brain activation during the fMRI tasks
- Task order, repeated twice per region: Reading, Picture, Recall, Picture
- Region stimulation counter-balanced

rTMS Selection and Data Analysis

Selection of rTMS Regions

- Regions were defined on a subject-specific basis, using an uncorrected threshold of $p < 0.05$
- The following contrasts was used to elicit activation

Lexical-semantic retrieval: picture - scrambled picture
Phonological encoding: nonword reading - consonant strings



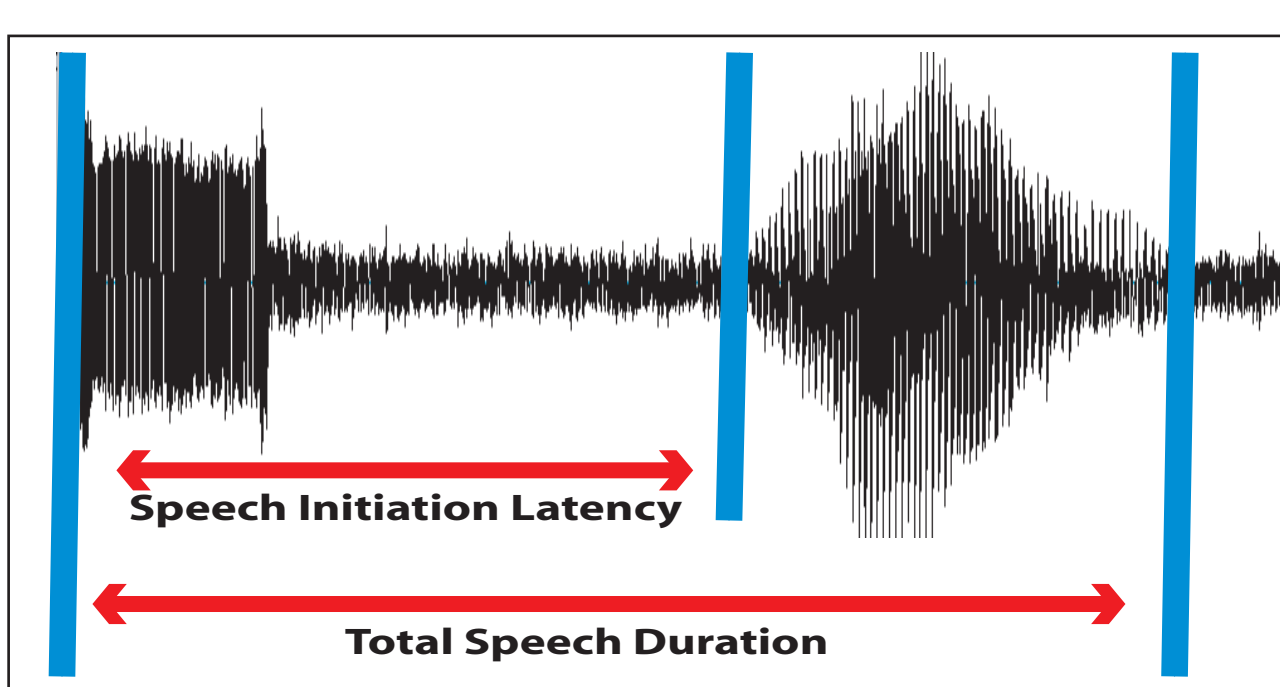
Posterior Superior Temporal Gyrus (pSTG) = phonological encoding

Middle Temporal Gyrus (MTG) = lexical-semantic retrieval

Participants

14 participants (7 female) participated and were compensated at \$20/hr. Mean age was 24.5 (SD=4.2). Two participants were excluded due to an inability to complete the experiment.

Behavioral Analyses



Target Utterance: rel pel nel kel lel
Omission: rel pel ___ kel lel
Substitutions: rel nel pel kel lel

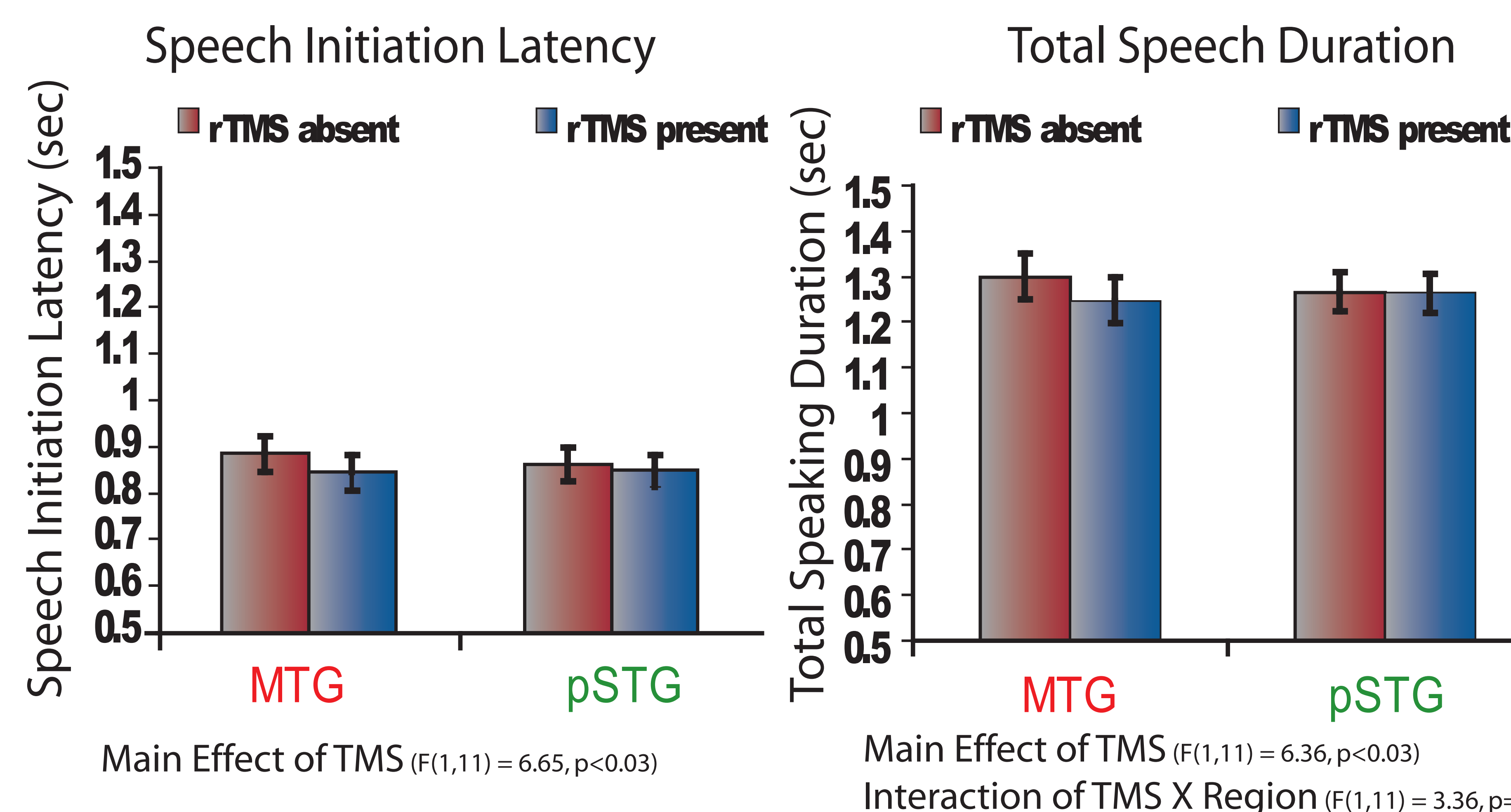
Speaking Times:

- Manually scored based on speech spectrogram
- Speech Initiation Latency = time from beginning of trial to begin speaking
- Total Speech Duration = time from beginning of the onset of speaking to finish speaking

Speech Error Analyses:

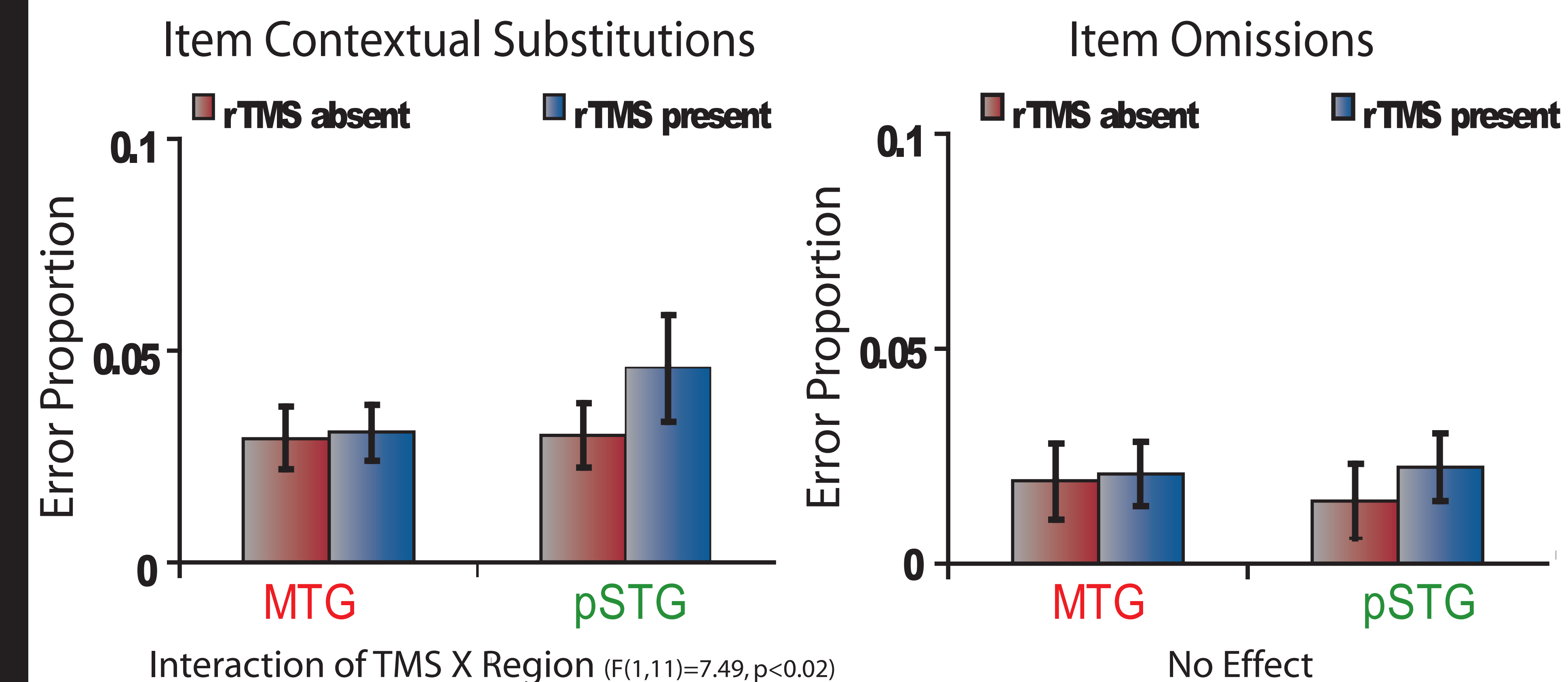
- Participant utterances were phonetically transcribed
- Two types of speech errors were coded for each item:
 - **Omissions** = leaving an item out of an utterance
 - **Substitutions** = substituting one item for another; only contextual substitutions (i.e., those from the target list) are reported

Results: Picture Naming



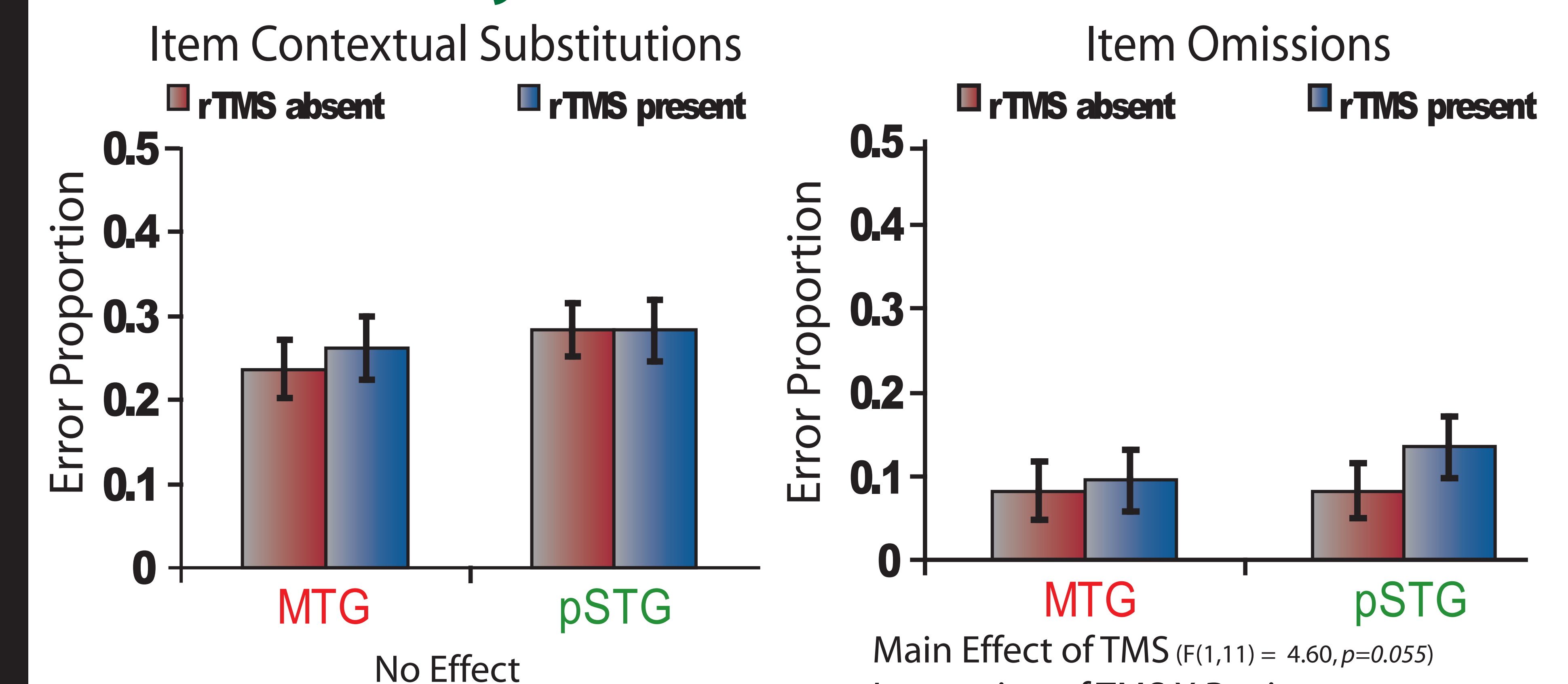
rTMS speeded speech initiation and speaking durations. This affect was not specific to the region being stimulated, but there was a trend for a TMS X Region interaction in Total Speech Duration in the expected direction (MTG > pSTG)

Results: Rapid Paced Reading



rTMS increased the number of speech errors (item contextual substitutions) when delivered to the pSTG but not the MTG

Results: Delayed Serial Recall



rTMS increased the number of speech errors (item omissions) when delivered to the pSTG but not the MTG

Conclusion

1. First study to show a direct, functional relationship between language production and verbal WM maintenance processes

Dissociation in the effect of rTMS on performance by region stimulated

pSTG - Increased error rate in serial recall and rapid-paced reading
- Faster speech initiation latency

MTG - No effect on error rates in serial recall and rapid-paced reading
- Faster speech onset and duration latencies

2. Results broadly consistent with previous demonstrations that WM is sensitive to rTMS of pSTG regions (e.g., Feredoes, Tononi & Postle, 2007; Kirschen, et al., 2006)

3. Results consistent with the emergent properties perspective on WM maintenance
- Although the type of speech error was different across WM (omission) and production tasks (substitutions), results confirmed that stimulation of regions involved in phonological encoding in production negatively impacts both production and WM tasks

3. Non-specific effects on picture naming tasks merit future research

- Similar results have been shown for pSTG (Mottaghey, Sparing & Topper, 2006) but not MTG
- Differences in regions could be explored through a chronometric method

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