Exploring the Relationship between Verbal Working Memory and Language Production using fMRI and TMS

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Introduction

Perspectives on Verbal Working Memory (WM) Maintenance

Specialized Systems

- WM maintenance achieved via langauge-independent storage systems (e..g the "phonological loop," Baddeley, 1986)
- Maintenance of verbal information localized in parietal regions (Paulesu, Frith & Frackowiak, 1993; Smith, Jonides, Marshuetz & Koeppe, 1998)

Emergent Properties

- WM maintenance achieved via temporary activation of long-term perception and action systems (Postle, 2006; Ruchkin, Grafman, Cameron & Berndty, 2003)
- Same regions of the brain associated with langauge perception and production will underlie WM maintenance (Buchsbaum & D'Esposito, 2008)
- *Language production hypothesis:* verbal WM maintenance achieved by the language production architecture (Acheson & MacDonald, 2008)

Present Study: Testing a Language Production-based Locus to WM Maintenance

1. Dissociate Sub-Processes of Language Production

- Language production dissociable into subprocesses associated with lexical-semantic retrieval (middle temporal gyrus; **MTG**) and the serial ordering of phonological elements (i.e."phonological encoding;" posterior superior temporal gyrus; **pSTG**; Indefrey & Levelt, 2004)

2. Target the pSTG and MTG for rTMS stimulation as people perform language production and memory tasks

- Use stimuli that lack semantic content (i.e., nonwords) that are likely to induce speech errors (i.e., phonologically similar items)

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

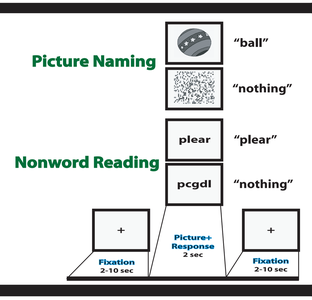
Design: Rapid Event-Related, with random stiumulus presentation jittered in time
ISIs ranged between 4-12 seconds

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)

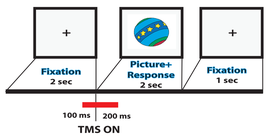
Data Analysis:
BOLD response was modeled using AFNI Gamma functions (GAM)



rTMS Procedure

Picture Naming

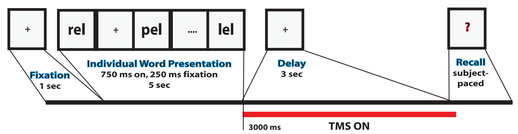
- **Participants named color pictures of common objects (Rossion & Pourtis, 2004)**
- **rTMS designed to target lexical-semantic access, occurring 100 ms prior through 200 ms after stimulus onset (4 pulses; Indefrey & Levelt, 2004)**
- **80 trials per region**



- 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

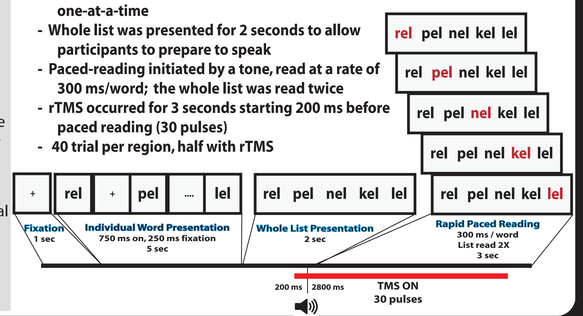
Delayed Serial Recall

- **Participants read a ist of 5 rhyming nonwords outloud 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/word; 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**

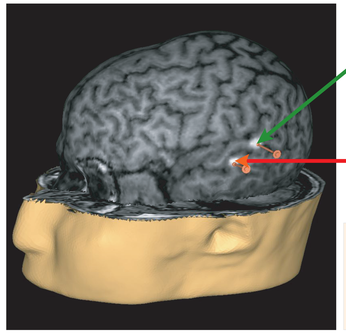


rTMS Selection and Data Analysis

Selection of rTMS Regions

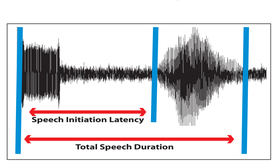
- Regions were defined on a subject-specific basis, using an uncorrected threshold of p<0.05
- The following contrast was used to elicit activation for lexical-semantic (positive values) and phonological encoding (negative values) processes:

[picture - scrambled picture] - [nonword reading - consonant strings]



Participants
13 participants (6 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

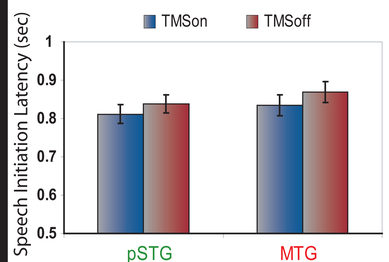
Speaking Times:
- Manually scored based on speech spectrogram
- Speech Initiation Latency = time from beginning of trial to begin speaking
- Total Speech Duration = time from beginning of the onset of speaking to finish speaking

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

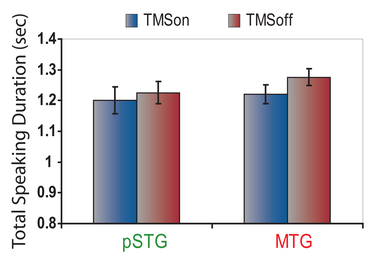
Collapsing across 1- and 2-syllable words: No Effect
Analysis was restricted to1-syllable words.

One-Syllable Word Speech Initiation Latency



Main Effect of TMS ($F(1,10) = 10.43, p<0.01$)

One-Syllable Word Total Speech Duration

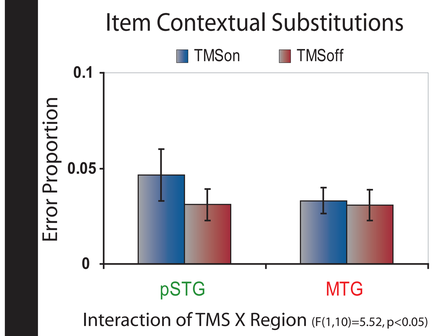


Main Effect of TMS ($F(1,10) = 5.75, p<0.05$)

Effect of TMS that was not specific to either region. TMS speeded speech initiation and speaking durations for one-syllable words only.

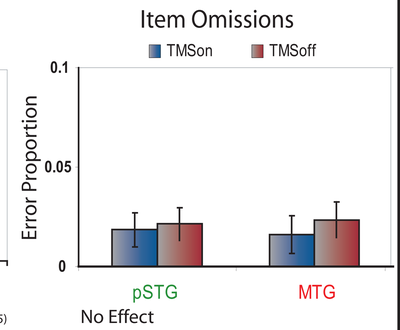
Results: Rapid Paced Reading

Item Contextual Substitutions



Interaction of TMS X Region ($F(1,10)=5.52, p<0.05$)

Item Omissions

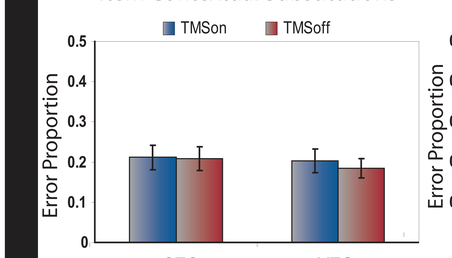


No Effect

TMS increased the number of speech errors (item contextual substitutions) for the pSTG but not the MTG

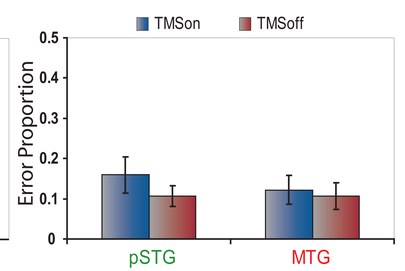
Results: Delayed Serial Recall

Item Contextual Substitutions



No Effect

Item Omissions



Main Effect of TMS ($F(1,10) = 4.29, p=0.07$)
Interaction of TMS X Region ($F(1,10)=4.52, p=0.06$)

TMS increased the number of speech errors (item omissions) for 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 onset and duration latencies for 1-syllable words

MTG - ***No*** effect on error rates in serial recall and rapid-paced reading
- Faster speech onset and duration latencies for 1-syllable words

2. 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

- could be a simple orienting response or rTMS stimulation using these timing parameter may have been affecting both phonological encoding and lexical-semantic retrieval.

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