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Short theta burst stimulation to left frontal cortex prior to encoding enhances subsequent recognition memory

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Abstract Deep semantic encoding of verbal stimuli can aid in later successful retrieval of those stimuli from long-term episodic memory. Evidence from numerous neuropsychological and neuroimaging experiments demonstrate regions in left prefrontal cortex, including left dorsolateral prefrontal cortex (DLPFC), are important for processes related to encoding. Here, we investigated the relationship between left DLPFC activity during encoding and successful subsequent memory with transcranial magnetic stimulation (TMS). In a pair of experiments using a 2-session within-subjects design, we stimulated either left DLPFC or a control region (Vertex) with a single 2-s train of short theta burst stimulation (sTBS) during a semantic encoding task and then gave participants a recognition memory test. We found that subsequent memory was enhanced on the day left DLPFC was stimulated, relative to the day Vertex was stimulated, and that DLPFC stimulation also increased participants' confidence in their decisions during the recognition task. We also explored the time course of how long the effects of sTBS persisted. Our data suggest 2 s of sTBS to left DLPFC is capable of enhancing subsequent memory for items encoded up to 15 s following stimulation. Collectively, these data demonstrate sTBS is capable of enhancing long-term memory and provide evidence that TBS protocols are a potentially powerful tool for modulating cognitive function.

Keywords Episodic memory · TMS · Prefrontal cortex · Recollection

Data from numerous neuropsychological and neuroimaging studies implicate the prefrontal cortex (PFC) in semantic encoding and the cognitive control processes that support successful long-term memory (for reviews, see Blumenfeld & Ranganath, 2007; Cabeza & Nyberg, 2000; Shimamura, 1995; Stuss & Benson, 1984). Neuroimaging studies show regions in left prefrontal cortex (PFC), including both dorsolateral (DLPFC) and ventrolateral prefrontal cortex (VLPFC), show higher levels of activation during deep, semantic encoding tasks compared to nonsemantic, phonological, or perceptual encoding tasks (e.g., Kapur et al., 1994; Otten, Henson, & Rugg, 2001; Petersen, Fox, Posner, Mintun, & Raichle, 1988). VLPFC activation during semantic encoding is higher for items that are later successfully remembered than for items that are later forgotten (Wagner et al., 1998). This has led to the suggestion that VLPFC activity reflects the selection of item-specific information that facilitates encoding of specific items rather than general distinctions. In contrast, the DLPFC's role in encoding processes is somewhat more debated. Rather than a direct role in encoding items, some studies suggest the DLPFC selects and organizes items to be encoded (e.g., Simons & Spiers, 2003) and others suggest a role for processing and encoding the relationships among items (e.g., Addis & McAndrews, 2006; Blumenfeld, Parks, Yonelinas, & Ranganath, 2010; Blumenfeld & Ranganath, 2006; Bor, Duncan, Wiseman, & Owen, 2003) or for the top-down modulation of posterior brain regions that represent information to be encoded, such as visual cortex (Gazzaley et al., 2007). The

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evidence is also mixed on whether DLPFC activation during encoding correlates with subsequent long-term memory. For example, Daselaar, Prince, and Cabeza (2004) and Otten and Rugg (2001) found either no correlation or a negative correlation between DLPFC activation and subsequent memory, but others—such as Murray and Ranganath (2007), Staresina and Davachi (2006), and Summerfield et al. (2006)—have found DLPFC activation positively correlated with successful subsequent memory performance.

Although the neuroimaging literature strongly implicates left frontal regions in semantic encoding, these data are correlational in nature and do not establish causal relationships between activation and subsequent memory performance. Complimentary brain stimulation methods to manipulate activity of prefrontal cortex, such as transcranial magnetic stimulation (TMS), have demonstrated that disrupting left prefrontal cortical activity prior to or during encoding disrupts subsequent memory performance (see Floel & Cohen, 2007, for a review), supporting the conclusion that left PFC is necessary to subsequent memory. In particular, Köhler, Paus, Buckner, and Milner (2004) found that short trains of 7 Hz repetitive TMS to a region in left inferior PFC during semantic encoding led to improvements in subsequent recognition memory for stimulated items, compared to items encoded while stimulating control sites. In contrast, Innocenti et al. (2010) found that short trains of 10 Hz repetitive TMS over left DLPFC reduced participants' accuracy and increased their reaction times for items encoded with deep encoding strategies. Consistent with the dissociation of ventral and dorsal areas of prefrontal cortex, Blumenfeld, Lee, and D'Esposito (2014) demonstrated reduced memory following continuous theta burst stimulation (TBS), a variant of repetitive TMS known to suppress motor cortical excitability (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005), over a region in left VLPFC prior to semantic encoding of word stimuli. In contrast, continuous TBS over DLPFC did not have a robust effect on encoding of word stimuli. Interestingly, the reduction in subsequent memory following stimulation of VLPFC was driven by an increase in false alarm rate during the retrieval. The increased false alarm rate supports the VLPFC's role in extracting and encoding specific semantic information about the word that would subsequently help in rejecting related foils during retrieval. The absence of a robust effect following DLPFC stimulation might suggest that DLPFC is not involved in long-term memory encoding. However, a robust effect following DLPFC stimulation might not be expected if other areas involved in organizing and relating information to be encoded were able to compensate for the continuous TBS-induced reduction in DLFPC activity. Instead, enhancing DLPFC cortical activity prior to encoding may provide unique insight into its role and possible clinical significance in long-term memory encoding. Enhancing DLPFC activity may improve subsequent recall and the confidence of recall by increasing relationships between subsequent words even if no intrinsic relationship exists.

Here, we sought to add to the relatively small, but growing, literature demonstrating that TMS can enhance cognitive function by investigating whether TMS to left DLPFC prior to semantic encoding could enhance subsequent recognition memory. We chose to use a short TBS (sTBS) protocol (Huang et al., 2005), where a single 2-s train of TBS is applied to the scalp. For about 15 s following stimulation, sTBS has been show to facilitate motor-evoked potentials (Huang et al., 2005), and the aftereffects of TBS protocols are NMDA receptor dependent, suggesting TBS is capable of affecting cellular mechanisms related to synaptic plasticity (Huang, Chen, Rothwell & Wen, 2007; Teo, Swayne, & Rothwell, 2007). To our knowledge, this is the first investigation of whether sTBS can enhance cognitive performance. We hypothesized that sTBS to left DLPFC during a semantic encoding task would facilitate DLPFC activity and lead to better subsequent long-term memory than memory for items encoded following sTBS to a control region. As a secondary line of investigation, we also wanted to explore the time course of sTBS's effects. To these ends, our first experiment followed a two-session, within-subjects design, where participants received sTBS during a semantic encoding task to either left DLPFC or to a control site and then completed a recognition memory test. For our second experiment, we sought to replicate and extend the findings from our first experiment by varying the timing between the sTBS application and the presentation of the word items during the semantic encoding task. Our findings support the hypothesis that sTBS to left DLPFC prior to encoding can improve subsequent long-term memory and provide evidence that TBS protocols can be useful for enhancing cognitive function.

Experiment 1

Method

Participants

Participants consisted of 18 young adults. Participants had normal or corrected-to-normal vision and did not report any conditions known to affect attention and memory. All participants were right-handed, as determined by the Edinburgh Handedness Scale (Oldfield, 1971). Participants were screened for TMS contradictions prior to the start of the experiment and were financially compensated at a rate of $15/hour. Two participants were excluded because of excessive sleepiness and/or failure to follow directions, leaving 16 participants in the analyzed dataset (ages 18 to 25 years, mean = 20.3 years). Participant recruitment and experimental

procedures were in accordance with protocols approved by the University of Michigan's Institutional Review Board.

Experimental design

Participants completed two experimental sessions. Both sessions were scheduled for the same time of day, and the second session was completed within 2 to 3 days of the first session. For each session, participants' resting and active motor thresholds were determined, and then participants performed an item-encoding task while receiving sTBS to either left DLPFC or Vertex. Participants received sTBS to only one site per session, and the stimulation site order was counterbalanced across participants. After completing the encoding task, participants had a 10-minute break followed by an item-recognition memory test.

TMS protocols

TMS was delivered with a MagPro X 100 with option stimulator (MagVenture Inc., Atlanta, GA) and a statically cooled figure-eight coil (MCF-B70). Prior to the start of the experiment, motor evoked potentials (MEPs) were used to determine the coil position that evoked the maximal response in the right first dorsal interosseous (FDI) muscle. The location and trajectory of the coil over left primary motor cortex (M1) were marked on the scalp, and this location was measured relative to scalp landmarks in order to minimize variability within and across sessions. Resting motor threshold was determined for each participant as the percentage of stimulator output that elicited an MEP of ≥50 μV peak to peak on 5 out of 10 trials. Active motor threshold (AMT) was determined as the percentage of stimulator output that elicited an MEP of ≥200 μV peak to peak on 5 out of 10 trials while participants maintained contraction of the right FDI at 20 % of maximal voluntary force.

For the left DLPFC stimulation site, the F3 electrode position from the International 10-20 system for the standardized placement of electroencephalogram (EEG) electrodes was used (Jasper, 1958). The TMS coil was placed tangentially to the scalp at this location, with the handle at 45 degrees to the midline in a posterior lateral orientation. For the Vertex control stimulation site, the Cz electrode position from the International 10-20 system was used, and the coil was placed tangentially to the scalp with the handle posterior and aligned with the midline. Short theta burst stimulation consisted of three pulses of stimulation, delivered at 50 Hz and an intensity of 80 % of AMT, and repeated every 200 ms for 2 s (Huang et al., 2005).

Item-encoding task

Experimental stimuli were presented using custom LabView software (National Instruments Co., Austin, TX) on a monitor positioned at eye level in front of the participants. For the item-encoding task, six lists of 60 nouns each were constructed. For each list, half of the words were concrete and half were abstract. Lists were matched for mean concreteness rating, written frequency, and word length. Three lists were used per session, and the lists used for each session were counterbalanced across participants. For each trial of the item-encoding task, participants received 2 s of sTBS and then viewed three nouns sequentially, one item from each of the three word lists used for the session. The first item was presented 700 ms following the 2-s stimulation. Each item was presented for 1,500 ms, with 700 ms of fixation between items (see Fig. 1). In order to encourage deep, semantic processing (Craik & Lockhart, 1972), participants were asked to think about the meaning of each word and to button-press to indicate whether the word was concrete or abstract. Participants were then presented with a fixation cross for 10 s prior to the onset of the next sTBS train. There were 60 trials in total. Following completion of the item-encoding task, participants took a 10-min break and then completed the item-recognition test.

Item-recognition test

The item-recognition test was a self-paced recognition memory task where participants were shown all 180 nouns from the item-encoding task and 180 new lure nouns. Word order was randomized. For each word, participants were asked to button-press to indicate whether the word was studied or unstudied and to indicate how confident they were of their decision (low or high confidence). This was done as a one-step procedure with four buttons (old item + high confidence, old item + low confidence, new item + high confidence, new item + low confidence).

Statistical analyses

For the encoding-phase data, participants' accuracy and reaction times for making the concrete/abstract decision were analyzed using a within-subjects repeated-measures ANOVA,

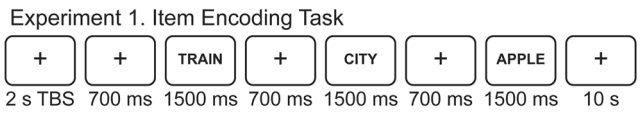

Fig. 1 Item-encoding task. Each trial of the encoding task began with participants receiving 2 s of sTBS to either left DLPFC or to the Vertex while they watched a fixation cross on a computer screen set up in front of them. Following the cessation of the sTBS, participants viewed three nouns sequentially on the screen. For each item (1,500 ms per item, with 700 ms of fixation between items), participants were asked to think about the meaning of the word and to make a button-press response to indicate whether the item was best categorized as concrete or abstract. Each trial ended with 10 s of fixation. There were 60 trials in total

with the factors of Stimulation Site (DLPFC, Vertex) and Delay Position within the trial, meaning the delay time between the offset of the sTBS and the onset of a noun, Delay 1 (700 ms), Delay 2 (2,900 ms), Delay 3 (5,100 ms). For the item-recognition test data, d' scores were calculated based on participants' hit rate for correctly recognizing studied items and their false alarm rate for incorrectly recognizing lure items, $d' = z(\text{hits}) - z(\text{false alarms})$ (Green & Swets, 1966). We subsequently analyzed d' results using a within-subjects, repeated-measures ANOVA with the factors of Stimulation Site (DLPFC, Vertex) and Delay Position (Delay 1, Delay 2, Delay 3). A follow-up Stimulation Site by Delay Position ANOVA was conducted on the hit data as well as a paired t test comparing false alarms for lure items in the DLPFC session and the Vertex session. Identical analyses were conducted on the high confidence responses, and the proportion of responses designated as high confidence were analyzed with a Stimulation Site by Delay Position repeated-measures ANOVA. For all analyses, the Huynh-Feldt sphericity correction was applied as needed. Corrected F and p values are reported, but degrees of freedom are rounded to integer values for easier reading. A priori hypotheses as well as significant ANOVA main effects and interactions were further queried using post hoc t tests.

Results and discussion

Site of sTBS does not affect decision-making accuracy or reaction times during item-encoding task

Figure 2 shows participants' accuracy and reaction times for making the abstract or concrete decision for each noun presented during the item-encoding task. For participants' accuracy, there was no interaction between Site and Delay Position, and no main effect of Site (both ps > .52, $\eta_p^2 < 0.04$). There was a significant main effect of Delay Position, $F(2, 30) = 1.84$, $p = .01$, $\eta_p^2 = 0.28$, with higher accuracy for items presented at Delay 3 than at Delay 1 ($p = .01$). Participants' reaction times during this encoding task followed a similar pattern as the accuracy results, with no interaction present between Site and Delay Position and no main effect of Site (both ps > .39, $\eta_p^2 < 0.05$). There was a main effect of Delay Position, $F(2, 30) = 28.15$, $p < .0001$, $\eta_p^2 = 0.65$, with participants' responding faster for items presented at Delays 2 and 3 than for items presented at Delay 1 (both ps < .001). Together, these data suggest that participants' ability to complete the concrete or abstract decision-making task was unaffected by the site of sTBS. Participants may have been slower and less accurate at responding to the first item in the trial sequence because it came relatively quickly after the offset of the stimulation, and they may not have been as prepared for this item as they were for later items.

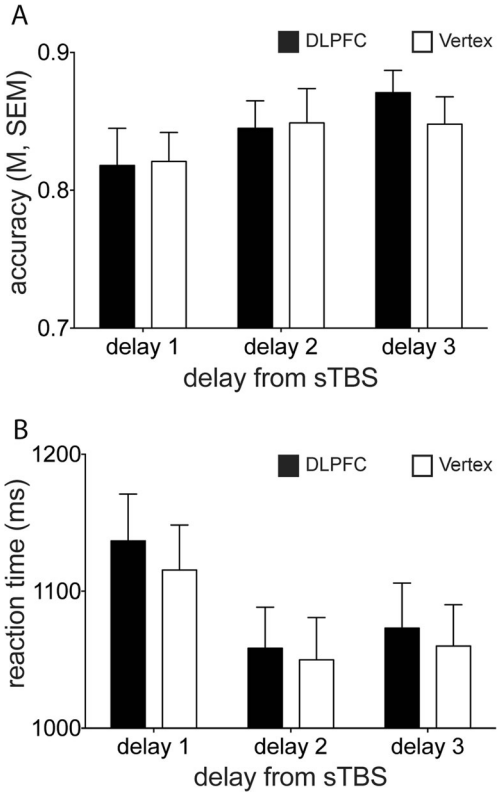

Fig. 2 Stimulation site does not affect accuracy or reaction times during item-encoding task. **a** The bars show the mean proportion of items correctly judged as concrete or abstract during the encoding phase of the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the between-subjects standard error around the mean. Stimulation site did not affect participants' decision accuracy during the encoding phase of Experiment 1. Participants were slightly better at determining whether the words presented at Delay 3 were either abstract concepts or concrete items than for the words presented at Delays 1 or 2. **b** Bars represent the mean reaction times for responses during the item encoding task for the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the standard error around the mean. Site of sTBS did not affect participants' reaction times, although for both sites participants were slower in responding to the first item (Delay 1) in the sequence than they were for the other two items in the trial

Left DLPFC stimulation enhances subsequent memory for studied items

Figure 3 depicts the d' results for the item-recognition task where participants were asked to decide whether a given item was studied (old) or unstudied (new). Critically, participants' d' scores were significantly higher on days where they received left DLPFC stimulation than on days where they received stimulation to Vertex, $F(1,15) = 7.69$, $p = .01$, $\eta_p^2 = 0.34$. Paired t tests between DLPFC and Vertex results revealed d' scores were significantly higher for DLPFC data for each of three Delay Positions (all ps < .04). The interaction between Site and Delay Position was not significant, $F(1, 15) = 0.24$, $p = .79$, $\eta_p^2 = 0.06$, and there was no significant main effect of Delay Position.

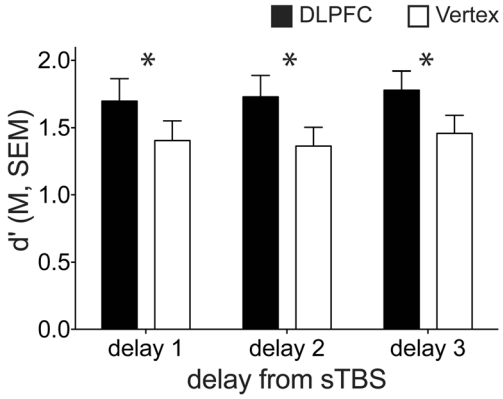

Fig. 3 During item-recognition test, sTBS to left DLPFC improves d′ scores. Bars represent the mean d′ scores for the recognition test during the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the between-subjects standard error around the mean. Asterisks denote paired *t* tests between DLPFC and Vertex bars significant at $p < .05$. For the item-recognition test, d′ scores were significantly higher on the day left DLPFC was stimulated during the encoding phase of the experiment than when the control site Vertex was stimulated. During each encoding trial (Delay 1, 2 or 3), d′ scores did not change as a function of when a studied item was presented

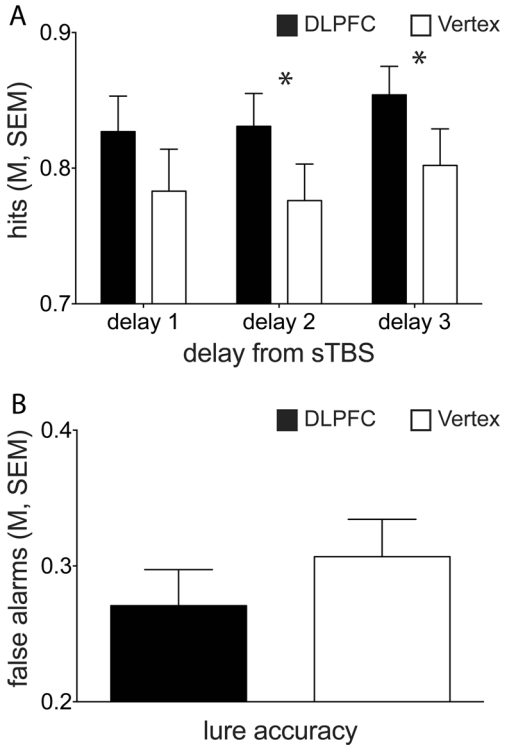

Fig. 4 Left DLPFC stimulation prior to encoding enhances subsequent item recognition. **a** Bars represent the mean proportion of hits (correct responses) to studied items during the item-recognition test for the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars are the between-subjects standard error around the mean. Asterisks denote paired *t* tests between DLPFC and Vertex bars significant at $p < .05$. Participants were better at correctly recognizing studied items when left DLPFC had been stimulated during the encoding phase than when Vertex was stimulated. **b** Bars represent the mean proportion of false alarms to lure (unstudied) items during the item-recognition test. Error bars are between-subjects standard errors around the mean. Participants' false alarms to lure items numerically decreased on the day DLPFC was stimulated, but this effect was not statistically significant

We further probed the recognition test results by separately analyzing the hit and false alarm data (Fig. 4a and b, respectively). For hits, Site and Delay Position did not interact, $F(2, 30) = 0.13$, $p = .88$, $\eta_p^2 = 0.01$. Importantly, participants' hit rate for studied items was higher in the DLPFC session than in the Vertex session, main effect of Site, $F(1, 15) = 9.10$, $p = .01$, $\eta_p^2 = 0.38$. Paired *t* tests between DLPFC and Vertex for each of the three Delay Positions revealed participants' hit rate was higher in the DLPFC session than in the Vertex session for items presented at Delays 2 and 3 (both $ps < .03$), but hit rates for Delay 1 did not differ between sessions, $t(15) = 1.96$, $p = .07$. There was also a main effect of Delay Position, $F(2, 30) = 3.41$, $p = .05$, $\eta_p^2 = 0.19$, such that participants were slightly better at remembering items that had been presented during the encoding task at Delay 3 than at Delay 1 or 2 (both $ps < .04$). Analysis of the lure data revealed that stimulating left DLPFC numerically lowered the proportion of false alarms participants had for lure items compared to stimulating Vertex, but this effect was not significant, $t(15) = 1.75$, $p = .10$, Cohen's $d = 0.44$. Thus, the boost to the *d′* scores on the day of DLPFC stimulation was primarily achieved by improving participants' ability to successfully recognize studied items rather than by improving their ability to reject lure items.

Participants are more confident they recognize studied items following left DLPFC stimulation

We next analyzed the responses from the item recognition test where participants indicated they had high confidence in their decision about whether a given item was studied (old) or unstudied (new; see Table 1). We first examined how Stimulation Site and Delay Position affected the proportion of high confidence hits. For these data, we controlled for participants' hit rate by counting the number of high confidence hit responses and dividing by the total number of hit responses. The overall proportion of hit items designated as high confidence increased during the DLPFC session compared to the Vertex session, main effect of Site, $F(1, 15) = 6.57$, $p = .02$, $\eta_p^2 = 0.31$. Paired *t* tests showed that for each of the three Delay Positions, the proportion of high confidence hits was higher on the DLPFC stimulation day than on the day Vertex was stimulated (all $ps < .03$). There was no main effect of Delay Position, and no interaction between Site and Delay Position for these data (both $ps > .28$). For lure items, there was no effect of Site on the proportion of false alarms to unstudied items rated as high confidence, $t(15) = 0.92$, $p = .37$, Cohen's $d = 0.23$.

Although *d′* scores were calculated based on high confidence hit and high confidence false alarm rates, there was no interaction between Site and Delay Position, $F(2, 30) = 0.66$, $p = .48$, $\eta_p^2 = 0.04$, or main effect of Site, $F(1, 15) = 0.31$, $p =$

Table 1 Experiment 1, data from responses rated as high confidence during item recognition test

DLPFC session					
Delay position	Items rated as high confidence hits (proportion)	Items rated as high confidence false alarms (proportion)	High confidence *d′* scores	Hit rate for high confidence items	False alarm rate for high confidence items
1	0.83 (0.04)	0.43 (0.06)	2.32 (0.17)	0.94 (0.02)	0.30 (0.05)
2	0.84 (0.03)		2.28 (0.19)	0.93 (0.02)	
3	0.86 (0.03)		2.41 (0.19)	0.95 (0.02)	
Vertex Session					
Delay position	Items rated as high confidence hits (proportion)	Items rated as high confidence false alarms (proportion)	High confidence *d′* scores	Hit rate for high confidence items	False alarm rate for high confidence items
1	0.79 (0.04)	0.40 (0.07)	2.31 (0.18)	0.95 (0.02)	0.32 (0.06)
2	0.78 (0.04)		2.26 (0.18)	0.95 (0.01)	
3	0.81 (0.04)		2.26 (0.19)	0.95 (0.01)	

Note. During the item recognition test, participants indicated whether each test item presented was studied (old) or unstudied (new) and gave a confidence rating (low, high) in their response. The data are the means (standard error around the means) for the items rated as high confidence during the DLPFC and Vertex sessions. Means based on studied item test data are separated based on which delay position the item was presented at within its encoding trial. We analyzed what proportion of correctly identified studied items (hits) were given a high confidence rating as well as the proportion of false alarms to lure items given a high confidence rating. For the test responses where participants indicated they were highly confident in their studied/unstudied judgment, we analyzed participants' accuracy (hits and false alarms) and calculated *d′* scores based on these rates

.59, $\eta_p^2 = 0.02$, or Delay Position, $F(2, 30) = 0.59$, $p = .56$, $\eta_p^2 = 0.04$. Similarly, there were no significant effects for the high confidence hit or high confidence false alarm data (all *p*s > .40, $\eta_p^2 < 0.05$). For the high confidence hits, participants' accuracy was close to ceiling for both the Vertex session and the DLPFC session (see Table 1 for means), meaning there was little room for improvements in accuracy. Thus, compared to the day Vertex was stimulated, DLPFC stimulation lead to a small increase in the proportion of studied items designated as high confidence hits. Looking exclusively at the high confidence responses, there were no differences between the DLPFC and Vertex sessions for the *d′* scores, hit rates, or false alarm rates.

Overall, the data from Experiment 1 suggest that sTBS to left DLPFC prior to encoding an item enhances participants' subsequent memory for those items. Because there were not interactions between the site of stimulation and when during the encoding trial an item was presented, it appears that any facilitatory effects from the DLPFC stimulation persisted for at least 5 s after the offset of stimulation. Participants' confidence in their memory for studied items was also increased by sTBS to left DLPFC , as evidenced by a higher proportion of accurate responses to studied test items being rated as high confidence.

Experiment 2

For Experiment 2, we wanted to assess the reproducibility of the findings from Experiment 1 and to assess how long the presumably facilitatory effects of sTBS to left DLPFC might last. To address these questions, Experiment 2 followed the same overall design as Experiment 1, but the word items within each trial of the item-encoding task were presented at a wider range of delays between the sTBS and the item presentation. We hypothesized that the effects of sTBS would diminish over time, meaning items encoded at longer delays following DLPFC stimulation would be less likely to show a subsequent memory enhancement.

Method

Participants

Experiment 2 consisted of 21 participants meeting the same criteria as in Experiment 1. Four participants were excluded due to excessive sleepiness or failure to follow experiment directions. This left 17 young adults (ages 18 to 24, mean = 19.9 years) for the final dataset.

Experimental design and TMS protocols

The overall experimental design and the TMS protocols were the same as those described for Experiment 1. For this experiment, the item-encoding task was altered in order to query longer delays between the sTBS and the presentation of a word to be encoded. As this change necessitated more items be used in the encoding task, more items were also presented here during the item-recognition task than in Experiment 1.

Item-encoding task

For Experiment 2, we assessed participants' subsequent memory for items that were encoded after longer delays following the sTBS than were used in Experiment 1. For each trial of the item encoding task (see Fig. 5), participants received 2 s of sTBS and then viewed three nouns sequentially. As in Experiment 1, participants were asked to button-press to indicate whether each word was concrete or abstract. Each word was presented for 1,500 ms. The first item was always presented 700 ms following stimulation (replicating the first Delay Position used in Experiment 1), but the amount of fixation before item 2 and before item 3 was varied across trials in order to query delays of approximately 5 s, 7 s, 11 s, and 15 s after the offset of the sTBS (5 Delay Positions total; see Table 2 for additional details on trial timings). The 5-s delay interval approximately replicated the Delay Period 3 (5,100 ms) used in Experiment 1, while the other delays allowed us to further query the time course of the effects of DLPFC stimulation on subsequent memory. As we did not observe in Experiment 1 any cumulative effects that would suggest a "build-up" of sTBS's effects over time (e.g., better subsequent memory for items presented in the second half of the encoding task than for items presented in the first half; unreported data), the fixation washout period at the end of each trial was shortened to 5 s. There were 84 trials total, with 84 items encoded at Delay Position 1 (700 ms) and 42 items encoded at all subsequent Delay Positions. This ensured we had sufficient trials to replicate the memory boost following DLPFC stimulation at least at Delay Position 1 while keeping the overall number of items reasonably constrained.

Ten new lists of nouns were constructed for this experiment. Five lists were used per session (one list per Delay Position), and the lists were counterbalanced across participants. The first list contained 84 items and the remaining lists contained 42 items each (252 words in total). As in Experiment 1, half of the words on each list were concrete and half were abstract, and lists were matched for mean concreteness rating, written frequency, and word length. Following completion of the item encoding task, participants took a 10-min break and then completed the item-recognition test.

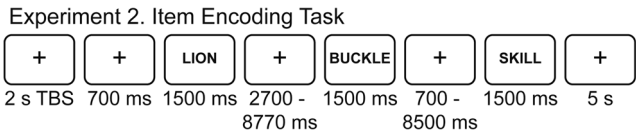

Fig. 5 Experiment 2, item-encoding task. As in Experiment 1, participants received 2 s of sTBS at the start of each trial and were then presented with three nouns. For each word, participants were asked to think about the meaning of the word and to button-press to indicate whether the word represented a concrete object or an abstract concept. For Experiment 2, the amount of fixation in between items 1 and 2 and items 2 and 3 was varied in order to query five possible delays between an item presentation and the sTBS at the start of the trial (approximately 700 ms, 5 s, 7 s, 11 s, or 15 s; see Table 2). Each trial ended with 5 s of fixation, and there were 84 trials in total

Item-recognition test

Procedures for the item-recognition task were similar to those used for Experiment 1. Participants completed a self-paced recognition memory task for 504 words (the 252 studied items and 252 lure words not previously presented). For each item, participants button-pressed to indicate whether the item was studied (old) or unstudied (new) and gave a confidence rating (low, high) in their decision.

Statistical analyses

Analysis procedures generally followed those used for Experiment 1. Within-subjects, repeated-measures ANOVAs used the factors of Stimulation Site (DLPFC, Vertex) and Delay Position (Delay 1, 2, 3, 4 and 5).

Results and discussion

Site of sTBS does not affect decision-making accuracy or reaction times during item-encoding task

As in Experiment 1, for participants' accuracy at making the abstract or concrete judgments during the encoding task, there was no interaction between Site and Delay Position, $F(4, 64) = 0.68$, $p = .57$, $\eta_p^2 = 0.04$. Here, there was a very strong trend for an effect of Site, $F(1, 16) = 4.42$, $p = 0.052$, $\eta_p^2 = 0.22$; DLPFC session mean accuracy: 0.79 ± 0.02, Vertex session accuracy: 0.75 ± 0.02 (see Fig. 6a). The effect of Delay Position was significant, $F(4, 64) = 3.28$, $p = .04$, 0.17, but there was not a clear pattern to the accuracy data across the Delay Positions (Delay Positions 2 and 4 showed the highest accuracy).

Reaction times did not vary as a function of Site or Delay Position and there was no interaction between these two factors (all Fs < 2.16, ps > .08, $\eta_p^2 < 0.12$; see Fig. 6b).

Left DLPFC stimulation prior to encoding increases d' scores in the memory-recognition test

Figure 7 shows the d' scores for the Experiment 2 item-recognition test. Replicating the findings from Experiment 1, participants' scores on the day they received left DLPFC stimulation immediately prior to encoding were significantly higher than when they received stimulation to Vertex, $F(1, 16) = 6.56$, $p = 0.02$, $\eta_p^2 = 0.29$. Paired t tests between DLPFC and Vertex d' scores revealed the scores were significantly higher on

Table 2 Trial parameters for Experiment 2, item encoding task.

Trial type	Fixation 1	Word 1	Fixation 2	Word 2	Fixation 3	Word 3	Delay
1	700	1,500	2,770	1,500	700	1,500	5,000
2	700	1,500	2,770	1,500	5,500	1,500	5,000
3	700	1,500	2,770	1,500	8,500	1,500	5,000
4	700	1,500	4,770	1,500	2,500	1,500	5,000
5	700	1,500	4,770	1,500	6,500	1,500	5,000
6	700	1,500	8,770	1,500	2,500	1,500	5,000

Note. For this experiment, longer delay intervals between the offset of the 2 s sTBS pulse and the onset of a word item were assessed. Six trial types with varying amounts of fixation in between Word 1 and Word 2, and Words 2 and 3 were constructed in order to query five possible delay positions (approximately 700 ms, 5 s, 7 s, 11 s, or 15 s following the sTBS offset). These six trial types were pseudorandomized within the encoding task. The table lists the duration (ms) of each aspect of the encoding task trials

the day DLPFC was stimulated for Delay Positions 1, 3, and 5 (all $ps < .03$). There was no effect of Delay Position or interaction between Site and Delay Position (both $Fs < 0.82$, $ps > .52$, $\eta_p^2 < 0.05$).

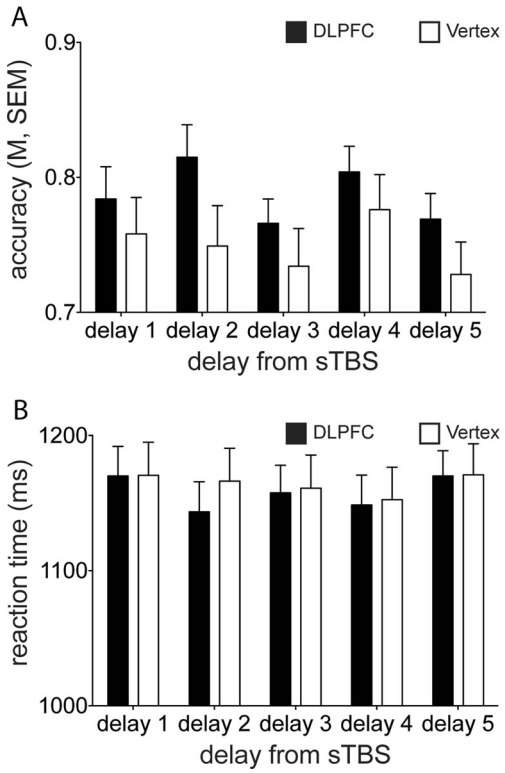

Fig. 6 Experiment 2, accuracy and reaction times for making the concrete or abstract judgment during the item encoding task. **a** The bars show the mean proportion of items correctly judged as concrete or abstract during the encoding phase of the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the between-subjects standard error around the mean. **b** The bars represent mean reaction times for responses during the item-encoding task for the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the standard error around the mean. There was a strong trend for higher accuracy when DLPFC was stimulated at the beginning of each trial compared to Vertex stimulation (see text for statistical details). Participants' reaction times during encoding did not significantly differ as a function of which site (DLPFC, Vertex) was stimulated

As in Experiment 1, the hit data for studied items during the recognition test did not show an interaction between Site and Delay Position, $F(4, 64) = 0.45$, $p = .73$, $\eta_p^2 = 0.03$, but there was an overall increase in hits on the day participants received DLPFC stimulation, $F(1, 16) = 10.02$, $p = .01$, $\eta_p^2 = 0.39$ (see Fig. 8a). Paired t tests showed hit rates were higher when DLPFC was stimulated than when Vertex was stimulated for items presented at Delays 1 and 3 (both $ps < .02$). In this experiment, the effect of Delay Position was not significant, $F(4, 64) = 0.89$, $p = .47$, $\eta_p^2 = 0.05$. For false alarms, as in Experiment 1, there was a numerical decrease on the day of DLPFC stimulation compared to the day of Vertex stimulation, but this effect was not statistically significant, $t(16) = 1.28$, $p = .22$, Cohen's $d = 0.31$ (see Fig. 8b).

Thus, these data replicate the effects of stimulation site found in Experiment 1. While we expected the effects of 2 s of TBS might be transient, the lack of a Site × Delay Position interaction for both the d' and hit data suggests the effects of sTBS last at least 15 s following stimulation.

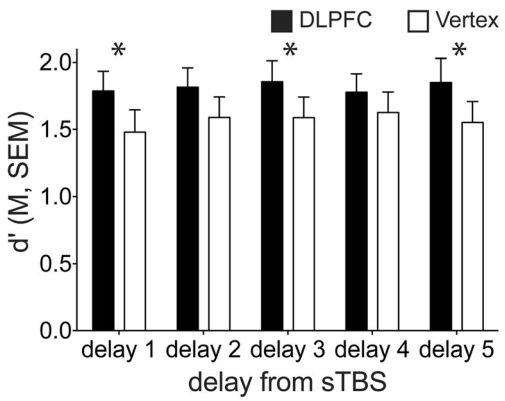

Fig. 7 Experiment 2, sTBS to left DLPFC prior to encoding enhanced d′ scores for the item-recognition test. Bars are the mean d′ scores for the recognition test during the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the between-subjects standard error around the mean. Asterisks denote paired t tests between DLPFC and Vertex bars significant at $p < .05$. Scores were significantly higher on the day left DLPFC was stimulated during encoding than when the Vertex was stimulated

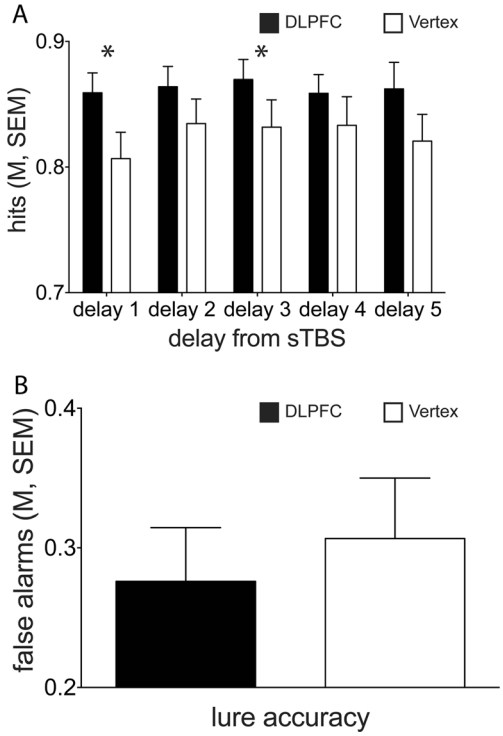

Fig. 8 Experiment 2, hit and false alarm rates for item-recognition test. **a** The bars represent the mean proportion of hits during the item-recognition test for the DLPFC session (*black bars*) and the Vertex session (*white bars*). Error bars represent the between-subjects standard error around the mean. Asterisks denote paired *t* tests between DLPFC and Vertex bars significant at $p < .05$. Participants' ability to correctly recognize studied items (hits) during the item-recognition test was enhanced on the day DLPFC was stimulated during the encoding task. **b** Bars represent the mean proportion of false alarms to lure (unstudied) items during the item-recognition test. Error bars are between-subjects standard errors around the mean. False alarms did not statistically differ between DLPFC and Vertex sessions

Participants are more confident they recognize studied items following left DLPFC stimulation

Replicating the site of stimulation effects seen in Experiment 1, the proportion of hit responses participants designated as high confidence was greater for the DLPFC session than for the Vertex session (see Table 3), main effect of Site, $F(1, 16) = 5.836$, $p = .03$, $\eta_p^2 = 0.27$. This was true for all five Delay Positions (paired *t* tests, all $ps < .05$). There was no effect of Delay Position or interaction between Site and Delay Position (both $Fs < 1.20$, $ps > 0.03$, $\eta_p^2 < 0.07$). For lure items, the proportion of false alarms designated as high confidence did not change as a function of Site, $t(16) = 1.87$, $p = .08$, Cohen's $d = 0.45$.

The *d′* scores calculated based on high confidence hit and false alarm rates showed a significant effect of Site, $F(1, 16) = 4.50$, $p = .05$, $\eta_p^2 = 0.22$, with higher *d′* scores on the DLPFC day (see Table 3 for means; paired *t* tests between Sites significantly different for Delays 1 and 5, both $ps < .05$). There was no significant effect of Delay Position or interaction between Site and Delay Position (both $Fs < 0.42$, $ps > 0.74$, $\eta_p^2 < 0.03$). High confidence hits were also higher on the day of DLPFC stimulation than on the day of Vertex stimulation, main effect of Site, $F(1, 16) = 5.26$, $p = .04$, $\eta_p^2 = 0.25$, paired *t* tests between Sites significant for Delays 1, 4 and 5, all $ps < .05$, but there was no effect of Delay Position or interaction between Site and Delay Position (both $Fs < 0.79$, $ps > 0.49$, $\eta_p^2 < 0.05$). High confidence false alarm rates for lure items also did not differ as a function of stimulation site, $t(16) = 0.27$, $p = .79$, Cohen's $d = 0.07$. Thus, as in Experiment 1, there was a higher proportion of high confidence hit responses during the DLPFC session. Here, the *d′* and hit rates calculated based on the responses rated as highly confident were significantly higher on the day of DLPFC stimulation.

General discussion

In both of our experiments, sTBS to left DLPFC during a semantic encoding task resulted in improved subsequent recognition memory, compared to stimulation of a control site (Vertex). This memory boost was evident both in the *d′* scores and in the hit data. We also found that DLPFC stimulation increased the proportion of high confidence hits participants reported. For Experiment 1, the delay between the offset of the sTBS and the presentation of a word item did not differentially affect the likelihood an item would be successfully remembered during the DLPFC session compared to the Vertex session. This suggested the effects of a single 2-s burst of TBS to DLPFC last at least 5 s. For Experiment 2, we further probed the time course of these effects by querying an extended range of delays between the stimulation offset and the presentation of an item to be encoded and found the effects of sTBS last at least 15 s following stimulation. These data fit with the observations of Huang et al. (2005) that 2 s of sTBS to motor cortex facilitated MEPs for roughly 15 s before returning to baseline. Future investigations will be needed to further probe how and for how long sTBS affects cortical excitability, both at our sites of stimulation and at other cortical regions.

To our knowledge, this is the first study to use sTBS to enhance cognitive function. Consistent with the increase in *d′* scores, increased hits for studied items, and increased confidence scores observed in our data during the DLPFC session, a few others have observed enhanced memory following TMS to left prefrontal cortex using other types of protocols, including increased hit rates (Köhler et al., 2004) and faster reaction times for studied items (Gagnon, Schneider, Grondin, & Blanchet, 2011). In our encoding data, there were no systematic, significant differences in reaction times or accuracy between the DLPFC session and the Vertex session, though Experiment 2 did show a very strong trend for higher accuracy following DLFPC stimulation. While session differences at the encoding phase were not critical to the hypotheses being

Table 3 Experiment 2, data from responses rated as high confidence during item recognition test

DLPFC session					
Delay position	Items rated as high confidence hits (proportion)	Items rated as high confidence false alarms (proportion)	High confidence *d′* scores	Hit rate for high confidence items	False alarm rate for high confidence items
1	0.79 (0.05)	0.48 (0.11)	2.55 (0.21)	0.96 (0.01)	0.30 (0.06)
2	0.78 (0.05)		2.56 (0.21)	0.96 (0.02)	
3	0.79 (0.05)		2.62 (0.20)	0.97 (0.01)	
4	0.79 (0.04)		2.55 (0.20)	0.96 (0.01)	
5	0.78 (0.05)		2.51 (0.24)	0.95 (0.01)	
Vertex session					
Delay position	Items rated as high confidence hits (proportion)	Items rated as high confidence false alarms (proportion)	High confidence *d′* scores	Hit rate for high confidence items	False alarm rate for high confidence items
1	0.67 (0.07)	0.30 (0.05)	2.11 (0.27)	0.87 (0.05)	0.31 (0.07)
2	0.62 (0.07)		2.13 (0.26)	0.87 (0.05)	
3	0.67 (0.07)		2.21 (0.25)	0.89 (0.04)	
4	0.67 (0.07)		2.23 (0.24)	0.90 (0.04)	
5	0.68 (0.07)		2.15 (0.25)	0.88 (0.04)	

Note. Data are the means (standard error around the means) for the proportion of hits to studied items given a high confidence rating; the proportion of false alarms to lure items given a high confidence rating; and the *d′* scores, hit, and false alarm rates calculated based on test items rated as high confidence. Data from the DLPFC session and the Vertex session are shown. Means based on studied item test data are separated based on the delay position the item was presented at within its encoding trial

tested here, the encoding data leave the door open for interpretation as to the mechanism underlying the boost in subsequent recognition memory. It is possible that DLPFC stimulation led to a better, more distinctive representation of each item during the encoding phase (as the trend for higher accuracy on the DLPFC day in Experiment 2 suggests). Alternatively, others have hypothesized that some behavioral improvements seen in the TMS literature are a result of an "addition-by-subtraction" mechanism, that is, enhancements in a process as a result of disrupting a region that competes with or detracts from that particular process (see review by Luber & Lisanby, 2014). Given this idea, as well as data from others showing that left DLPFC activity has also been observed for subsequently forgotten items (e.g., see review by Wagner & Davachi, 2001), it is possible that the better memory performance we observe could be the result of TBS disrupting DLPFC activity. Finally, an interesting possibility is that our experimental design increased the likelihood of participants using a relational strategy to encode study trial items, as we delivered sTBS prior to an encoding trial containing three items. In contrast, others have delivered TMS either during the presentation of encoding items (Köhler et al., 2004) or prior to the start of the encoding session (e.g., Blumenfeld et al., 2014). By breaking our stimulus lists into smaller sets of three, our design may have encouraged relational processing of encoding stimuli (Blumenfeld & Ranganath, 2007), which could have made the DLPFC cortical enhancement particularly beneficial. Further TBS work could explicitly manipulate the encoding task and materials in order to test whether enhancing DLPFC activity enhances the encoding of relationships between items.

Related to this question of mechanism, it is important to consider our experimental control of active Vertex stimulation and whether it sufficiently guards against the possibility that better test performance on DLPFC days was a result of a nonspecific mechanism (e.g., more arousal during encoding) related to the sound or physical sensation caused by delivery of the TBS pulses. Vertex stimulation produces the same auditory effects and scalp sensations as our DLPFC stimulation, but is an area of the brain (the leg/ foot region of motor cortex) unlikely to be important to the processes studied here. In contrast, using another frontal site as a control condition would be more likely to cause behavioral effects, as many frontal regions are implicated in the processes being tested here (e.g., see review by Fletcher & Henson, 2001). However, TMS to frontal sites like DLPFC can sometimes produce peripheral muscle stimulation and contraction of facial muscles, which can be mildly uncomfortable for participants. Although one would expect painful stimulation would reduce memory performance, there is also a small chance that the painful stimuli would be a superior alerting stimulus to the nonpainful stimulation of Vertex. However, our data did not support this explanation. In Experiment 1, three out of 16 participants reported or were observed to have visible facial muscle stimulation as a result of the TBS to DLPFC. Of these three, two participants performed slightly worse (numerically lower average *d′* score) on the DLPFC session memory test than on the Vertex session test, and 1 participant performed better on the DLPFC

day. Similarly in Experiment 2, one out of 17 participants reported facial muscle stimulation (participant performed better on DLPFC day). Overall, although there may be limitations to using Vertex stimulation as a control, it seems unlikely that our results of better memory test accuracy on the day of DLPFC stimulation were driven by systematic issues pertaining to the physical sensations caused by TBS to DLPFC.

In addition to understanding more about the cognitive and behavioral consequences of modulating DLPFC activity, it will also be important and interesting to investigate how stimulation of DLPFC can affect activity in downstream functionally or structurally connected brain regions. In a recent interleaved TMS–fMRI study, biphasic TMS pulses to the F3 scalp location or to a location above medial PFC were delivered while participants underwent an fMRI scan (Hanlon et al., 2013). Although stimulation of both sites increased activation of the cortex directly adjacent to the stimulation site as expected, this study also found an interaction between stimulation site and brain activation in several subcortical striatal regions. For example, F3 stimulation differentially activated the hippocampus compared to medial PFC stimulation, while medial PFC stimulation differentially activated the caudate. While preliminary, these data provide further evidence that stimulating different regions within the PFC can be used as a means to target functionally distinct cortical–subcortical networks. It is possible the key mechanisms underlying the benefits to subsequent memory seen in the current experiments were a result of changes to downstream subcortical brain regions connected to DLPFC. As clinical TMS treatments for depression and schizophrenia are also targeting left DLPFC (O'Reardon et al., 2007; Slotema, Blom, Hoek, & Sommer, 2010), and disruption of mesocortical and mesolimbic networks has been consistently demonstrated in these disorders, understanding the downstream effects of TMS will also be critical for uncovering the neural mechanisms underlying the clinical benefits seen from left DLFPC stimulation in these patient populations.

Our study used the F3 electrode location from the International 10-20 system for placing EEG electrodes as our means of targeting left DLPFC. While this location is widely used to target left DLPFC in basic science and clinical TMS studies, recent work has also made use of stereotaxic neuronavigation techniques (Paus, 1999) to coregister coordinates from individuals' structural or functional magnetic resonance images (MRIs) to a corresponding position on the scalp (e.g., Blumenfeld et al., 2014). Neuronavigated TMS studies may reduce interindividual variability and the number of participants necessary to sufficiently power a study (Sack et al., 2009) and will be critical for precisely and reliably targeting frontal subregions. However, collecting MR images on participants prior to collecting TMS data also adds to the cost and effort involved in conducting TMS research. Although collecting structural and/or functional MR data from our participants for neuronavigation purposes was not feasible in the current studies, we were nonetheless able to show significant behavioral effects following F3 stimulation. Importantly, our second experiment demonstrated that these effects were reproducible in an independent set of subjects. Given the tolerability of sTBS relative to other TMS protocols, our evidence F3 stimulation can enhance cognitive function in normal individuals, and the evidence from Hanlon et al. (2013) that F3 stimulation caused activation changes in a network of cortical and subcortical regions including hippocampus, sTBS to F3 could be an impactful target for clinical treatments to improve cognitive functioning in patient populations.

In summary, our data demonstrate that single, 2-s trains of TBS to left DLPFC immediately prior to the semantic encoding of words leads to better subsequent memory for those words than words encoded following Vertex stimulation. These data thus provide key causal evidence for the role of left DLPFC in long-term memory and demonstrate the usefulness of theta burst protocols for enhancing cognitive function in healthy adults.

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Compliance with ethical standards

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References

Addis, D. R., & McAndrews, M. P. (2006). Prefrontal and hippocampal contributions to the generation and binding of semantic associations during successful encoding. *NeuroImage, 33*(4), 1194–1206. doi:10.1016/j.neuroimage.2006.07.039

Blumenfeld, R. S., Lee, T. G., & D'Esposito, M. (2014). The effects of lateral prefrontal transcranial magnetic stimulation on item memory encoding. *Neuropsychologia, 53,* 197–202. doi:10.1016/j.neuropsychologia.2013.11.021

Blumenfeld, R. S., Parks, C. M., Yonelinas, A. P., & Ranganath, C. (2010). Putting the pieces together: The role of dorsolateral prefrontal cortex in relational memory encoding. *Journal of Cognitive Neuroscience, 23*(1), 257–265.

Blumenfeld, R. S., & Ranganath, C. (2006). Dorsolateral prefrontal cortex promotes long-term memory formation through its role in working memory organization. *Journal of Neuroscience, 26*(3), 916–925. doi:10.1523/JNEUROSCI.2353-05.2006

Blumenfeld, R. S., & Ranganath, C. (2007). Prefrontal cortex and long-term memory encoding: An integrative review of findings from neuropsychology and neuroimaging. *The Neuroscientist, 13*(3), 280–291. doi:10.1177/1073858407299290

Bor, D., Duncan, J., Wiseman, R. J., & Owen, A. M. (2003). Encoding strategies dissociate prefrontal activity from working memory demand. *Neuron, 37*(2), 361–367.

Cabeza, R., & Nyberg, L. (2000). Neural bases of learning and memory: Functional neuroimaging evidence. *Current Opinion in Neurology, 13*(4), 415–421.

Craik, F. I., & Lockhart, R. S. (1972). Levels of processing: A framework for memory research. *Journal of Verbal Learning & Verbal Behavior, 11*(6), 671–684. doi:10.1016/S0022-5371(72)80001-X

Daselaar, S. M., Prince, S. E., & Cabeza, R. (2004). When less means more: Deactivations during encoding that predict subsequent memory. *NeuroImage, 23*(3), 921–927. doi:10.1016/j.neuroimage.2004.07.031

Fletcher, P. C., & Henson, R. N. A. (2001). Frontal lobes and human memory: Insights from functional neuroimaging. *Brain, 124,* 849–881.

Floel, A., & Cohen, L. G. (2007). Contribution of noninvasive cortical stimulation to the study of memory functions. *Brain Research Reviews, 53*(2), 250–259. doi:10.1016/j.brainresrev.2006.08.006

Gagnon, G., Schneider, C., Grondin, S., & Blanchet, S. (2011). Enhancement of episodic memory in young and healthy adults: A paired-pulse TMS study on encoding and retrieval performance. *Neuroscience Letters, 488*(2), 138–142. doi:10.1016/j.neulet.2010.11.016

Gazzaley, A., Rissman, J., Cooney, J., Rutman, A., Seibert, T., Clapp, W., & D'Esposito, M. (2007). Functional interactions between prefrontal and visual association cortex contribute to top-down modulation of visual processing. *Cerebral Cortex, 17*(Suppl. 1), i125–i135. doi:10.1093/cercor/bhm113

Green, D. M., & Swets, J. A. (1966). *Signal detection theory and psychophysics*. New York: Wiley.

Hanlon, C. A., Canterberry, M., Taylor, J. J., DeVries, W., Li, X., Brown, T. R., & George, M. S. (2013). Probing the frontostriatal loops involved in executive and limbic processing via interleaved TMS and functional MRI at two prefrontal locations: A pilot study. *PLOS ONE, 8*(7), e67917. doi:10.1371/journal.pone.0067917

Huang, Y. Z., Chen, R. S., Rothwell, J. C., & Wen, H. Y. (2007). The after-effect of human theta burst stimulation is NMDA receptor dependent. *Clinical Neurophysiology, 118*(5), 1028–1032. doi:10.1016/j.clinph.2007.01.021

Huang, Y. Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta burst stimulation of the human motor cortex. *Neuron, 45*(2), 201–206. doi:10.1016/j.neuron.2004.12.033

Innocenti, I., Giovannelli, F., Cincotta, M., Feurra, M., Polizzotto, N. R., Bianco, G., . . . Rossi, S. (2010). Event-related rTMS at encoding affects differently deep and shallow memory traces. *NeuroImage, 53*(1), 325–330. doi:10.1016/j.neuroimage.2010.06.011

Jasper, H. H. (1958). The ten-twenty electrode system of the International Federation. *Electorencephalography and Clinical Neurophysiology, 10,* 370–375.

Kapur, S., Craik, F. I., Tulving, E., Wilson, A. A., Houle, S., & Brown, G. M. (1994). Neuroanatomical correlates of encoding in episodic memory: Levels of processing effect. *Proceedings of the National Academy of Sciences of the United States of America, 91*(6), 2008–2011.

Köhler, S., Paus, T., Buckner, R. L., & Milner, B. (2004). Effects of left inferior prefrontal stimulation on episodic memory formation: A two-stage fMRI–rTMS study. *Journal of Cognitive Neuroscience, 16*(2), 178–188.

Luber, B., & Lisanby, S. H. (2014). Enhancement of human cognitive performance using transcranial magnetic stimulation (TMS). *NeuroImage, 85,* 961–970. doi:10.1016/j.neuroimage.2013.06.007

Murray, L. J., & Ranganath, C. (2007). The dorsolateral prefrontal cortex contributes to successful relational memory encoding. *Journal of Neuroscience, 27*(20), 5515–5522. doi:10.1523/JNEUROSCI.0406-07.2007

O'Reardon, J. P., Solvason, H. B., Janicak, P. G., Sampson, S., Isenberg, K.E., Nahas, Z., . . . Sackeim, H. A. (2007). Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: A multisite randomized controlled trial. *Biological Psychiatry, 62*(11), 1208–1216. doi:10.1016/j.biopsych.2007.01.018

Oldfield, R. C. (1971). The assessment and analysis of handedness: Edinburgh inventory. *Neuropsychologia, 9,* 97–113.

Otten, L. J., Henson, R. N., & Rugg, M. D. (2001). Depth of processing effects on neural correlates of memory encoding: Relationship between findings from across- and within-task comparisons. *Brain, 124*(2), 399–412.

Otten, L. J., & Rugg, M. D. (2001). When more means less: Neural activity related to unsuccessful memory encoding. *Current Biology, 11*(19), 1528–1530.

Paus, T. (1999). Imaging the brain before, during, and after transcranial magnetic stimulation. *Neuropsychologia, 37*(2), 219–224.

Petersen, S. E., Fox, P. T., Posner, M. I., Mintun, M., & Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature, 331*(6157), 585–589.

Sack, A. T., Kadosh, R. C., Schuhmann, T., Moerel, M., Walsh, V., & Goebel, R. (2009). Optimizing functional accuracy of TMS in cognitive studies: A comparison of methods. *Journal of Cognitive Neuroscience, 21*(2), 207–221.

Shimamura, A. P. (1995). Memory and the prefrontal cortex. *Annals of the New York Academy of Sciences, 769,* 151–159.

Simons, J. S., & Spiers, H. J. (2003). Prefrontal and medial temporal lobe interactions in long-term memory. *Nature Reviews Neuroscience, 4*(8), 637–648. doi:10.1038/nrn1178

Slotema, C. W., Blom, J. D., Hoek, H. W., & Sommer, I. E. (2010). Should we expand the toolbox of psychiatric treatment methods to include repetitive transcranial magnetic stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. *Journal of Clinical Psychiatry, 71*(7), 873–884. doi:10.4088/JCP.08m04872gre

Staresina, B. P., & Davachi, L. (2006). Differential encoding mechanisms for subsequent associative recognition and free recall. *Journal of Neuroscience, 26*(36), 9162–9172. doi:10.1523/JNEUROSCI.2877-06.2006

Stuss, D. T., & Benson, D. F. (1984). Neuropsychological studies of the frontal lobes. *Psychological Bulletin, 95*(1), 3–28.

Summerfield, C., Greene, M., Wager, T., Egner, T., Hirsch, J., & Mangels, J. (2006). Neocortical connectivity during episodic memory formation. *PLOS Biology, 4*(5), e128. doi:10.1371/journal.pbio.0040128

Teo, J. T. H., Swayne, O. B., & Rothwell, J. C. (2007). Further evidence for NMDA-dependence of the after-effects of human theta burst stimulation. *Clinical Neurophysiology, 118*(7), 1649–1651. doi:10.1016/j.clinph.2007.04.010

Wagner, A. D., & Davachi, L. (2001). Cognitive neuroscience: Forgetting of things past. *Current Biology, 11,* R964–R967.

Wagner, A. D., Schacter, D. L., Rotte, M., Koutstaal, W., Maril, M., Dale, A. M., . . . Buckner, R. L. (1998). Building memories: remembering and forgetting of verbal experiences as predicted by brain activity. *Science, 281*(5380), 1188–1191.