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Left middle temporal and inferior frontal regions contribute to speed of lexical decision: A TMS study

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ABSTRACT

Activation of left anterior inferior frontal gyrus (aLIFG) and left middle temporal gyrus (LMTG) has been observed in some functional neuroimaging studies of lexical decision but not others. It is thus unclear whether these two regions are necessary for word recognition. By applying continuous theta-burst transcranial magnetic stimulation (TMS) which temporally suppresses local brain function, we examined whether aLIFG and LMTG play causal roles in word recognition in a visual lexical decision task (LDT). Furthermore, we manipulated stimulus onset asynchrony (SOA) between prime and target to test whether these regions contribute to word recognition differently. In the LDT task, target words were preceded by semantically related primes (Related Condition; RC) or semantically unrelated words (Unrelated Condition; UC), under both short (150 ms) and long (600 ms) SOA conditions. TMS of aLIFG and LMTG significantly affected the word recognition speed compared to TMS of Vertex. Our results provide evidence that both aLIFG and LMTG contribute to word recognition speed. Furthermore, at short SOA, TMS of aLIFG or LMTG prolonged reaction time (RT). In contrast, at long SOA, there was a significant region by SOA by TMS interaction such that TMS of aLIFG prolonged RT, whereas TMS of LMTG speeded RT. These results suggest that aLIFG and LMTG may play different roles in word recognition.

1. Introduction

Word recognition is critical for reading and language comprehension. Since the seminal functional neuroimaging studies of Petersen, Fox, Posner, Mintun, and Raichle (1988), a body of evidence has suggested that word recognition is supported by a fronto-temporal network (Lau, Phillips, & Poeppel, 2008; Price, 2012) as well as the interaction between fronto-temporal regions (Heim et al., 2009). Two specific brain regions which have garnered much discussion related to word recognition are the anterior–ventral portions of the left inferior frontal gyrus (aLIFG; ~Brodmann 47) and the left posterior middle temporal gyrus (LMTG; ~Brodmann 21) (Lau et al., 2008). However, the most consistently established finding concerning aLIFG and LMTG is that these regions are activated during explicit semantic decision tasks (Badre, Poldrack, Paré-Blagoev, Insler, & Wagner, 2005; Giesbrecht, Camblin, & Swaab, 2004), for both words and pictures (Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996).

In contrast, it is less clear if aLIFG and LMTG contribute to lexical processes that do not require explicit semantic decisions. Whereas some neuroimaging studies of word reading or lexical decision have reported activation of these regions (Bookheimer, Zeffiro, Blaxton, Gaillard, & Theodore, 1995; Fiez & Petersen, 1998; Heim et al., 2009; Madden et al., 2002), others have not (Gold, Andersen, Jicha, & Smith, 2009; Petersen et al., 1988). In addition, although large peri-Sylvian lesions tend to impair word recognition performance (Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004; Hagoort, 1993; Milberg & Blumstein, 1981; Swick, 1998), such lesions typically extend beyond the aLIFG or LMTG. For instance, a lack of priming related to ambiguous words has been observed in patients with lesions of left prefrontal cortex (Metzler, 2001). In addition, impaired visual word priming has been reported in patients with lesions of medial temporo-occipito cortex (Carlesimo, Fadda, Sabbadini, & Caltagirone, 1994; NielsenBohlman, Ciranni, Shimamura, & Knight, 1997). Lesions studies have further suggested that LMTG is important for word-level comprehension (Dronkers et al., 2004). However, focal lesions to aLIFG or LMTG are rare. In particular, selective lesions of aLIFG are rare because it is a watershed region that is supplied by branches from multiple cerebral arteries (middle and anterior

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cerebral arteries). Therefore, it is unclear whether aLIFG and LMTG are directly involved in lexical processes that do not involve explicit semantic decisions.

The main aim of the present study was to test whether the aLIFG and LMTG are causally involved in word recognition. This issue is of potential clinical relevance because word recognition is critical to comprehension of written language (Perfetti, 1994) and its impairment forms a central component of developmental reading disorders (Sigmundsson, 2005). If aLIFG and LMTG do contribute to word recognition then TMS-induced lesions of these regions should affect lexical decision performance. The advantage of TMS is that it can induce a temporary "virtual lesion" which may help establish the causality between an anatomical area and cognitive function. Indeed, TMS has been successfully used to investigate neural underpinnings of language (Cattaneo, Devlin, Salvini, Vecchi, & Silvanto, 2010; Cattaneo, Devlin, Vecchi, & Silvanto, 2009; Devlin & Watkins, 2007; Pulvermuller & Fadiga, 2010). For instance, suppression of language production has been reported when the left lateral prefrontal cortex was stimulated (Nardone et al., 2011) by continuous theta-burst TMS (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005).

A secondary aim of the present study was to address the issue of whether aLIFG and LMTG may play slightly different roles in word recognition by incorporating a semantic priming paradigm within our design. For example, several functional neuroimaging studies have reported semantic neural priming effects in regions at or near LMTG at short stimulus onset asynchrony (SOA), suggesting a role for LMTG in early stages of word recognition (Devlin, Jamison, Matthews, & Gonnerman, 2004; Gold & Rastle, 2007; Gold et al., 2006; Sass, Krach, Sachs, & Kircher, 2009; Wheatley, Weisberg, Beauchamp, & Martin, 2005). However, it remains unclear whether LMTG plays a role in the later stages of word recognition. Some studies have reported a semantic neural priming effect in LMTG at long SOA (Giesbrecht et al., 2004; Gold et al., 2006; Kuperberg, Lakshmanan, Greve, & West, 2008), while others have not (Matsumoto, Iidaka, Haneda, Okada, & Sadato, 2005; Rossell, Price, & Nobre, 2003). Similarly, although semantic priming effects at long SOA have been reported in aLIFG (Giesbrecht et al., 2004; Gold et al., 2006; Lau et al., 2008; Matsumoto et al., 2005), some studies have also reported semantic priming effects in aLIFG at short SOA (Copland et al., 2003; Dale et al., 2000; Liu, Hu, Peng, Yang, & Li, 2010; Shtyrov & Pulvermuller, 2007), while others have not (Devlin et al., 2004; Gold & Rastle, 2007; Gold et al., 2006; Sass et al., 2009; Wheatley et al., 2005).

In the present study, the aim was to test whether TMS produced an interference effect on word recognition and whether the TMS effect was region-specific. To test the TMS effect, we compared task performance between sessions with (TMS) and without TMS (Baseline). To test regional functional effects, we compared two TMS sites of interest (aLIFG and LMTG) and a control site (Vertex). To further explore potentially different roles of aLIFG and LMTG in word recognition, we manipulated the SOA in the context of a semantically primed lexical decision study. If aLIFG and LMTG are necessary for word recognition, then TMS interference of their functioning should affect behavioral performance compared to stimulation of Vertex. It should be noted that semantic priming at short SOA is dominated by automatic processes whereas semantic priming at long SOA involves additional strategic mechanisms which are associated with participant expectancies (Balota, Black, & Cheney, 1992). Therefore, if aLIFG and LMTG contribute to early/automatic stages of word recognition then lexical decision task (LDT) behavioral performance at short SOA should be disrupted when either region is stimulated. If either region contributes to the later/strategic stages of word recognition then LDT behavioral performance should be disrupted as a result of stimulation of that region at long SOA.

2. Methods and materials

2.1. Participants

A total of 28 native Chinese speakers participated in the present study. Sixteen participants (6 female) received TMS over the aLIFG (mean age = 25.2 years, range = 20–28 years), and twelve participants (3 female) received TMS over the LMTG (mean age = 23.1 years, age range = 19–27 years). All of the participants were right-handed with normal or corrected-to-normal vision. None of the participants reported neurological disorders or were taking medication at the time of the test. Written informed consent was obtained from each participant and this study was approved by the Ethics Committee of Chang-Gung Memorial Hospital, Taiwan.

2.2. Lexical decision task

For the lexical decision task (LDT), 384 triplet pairings were constructed. First, a target word (noun) was created and two additional words (both nouns) were selected and paired with the target word. One of the paired words was semantically related to the target word (Related Condition; RC) and the other word was semantically unrelated to the target word (Unrelated Condition; UC). Thus, each triplet included a target word, a related prime word and an unrelated prime word. The semantically related and unrelated words, which served as primes, were matched in terms of word frequency (RC 166.57 ± 15.28, UC 163.93 ± 16.16, t (383) = .45, p = .66) (according to Academia Sinica Balanced Corpus of Modern Chinese, Taiwan, http://rocling.iis.sinica.-edu.tw/CKIP/20corpus.htm) and stroke number (RC 20.44 ± 0.33, UC 20.97 ± 0.33, t (383) = 1.13, p = .26). A total of 48 young adults from the same subject pool whom did not participate in the study rated the familiarity, concreteness, imageability and semantic relatedness from 1 to 5 (12 subjects for each). The prime familiarity (5 for well familiar, RC 4.73 ± 0.01, UC 4.71 ± 0.01, t (383) = 1.37, p = .17), concreteness (5 for well concrete, RC 4.40 ± 0.03, UC 4.39 ± 0.03, t (383) = 0.30, p = .77), and imageability (5 for highly imageable, RC 4.00 ± 0.03, UC 4.01 ± 0.04, t (383) = 0.37, p = .71) were matched between the two conditions according to the rating. A significant difference between the RC and UC was observed with higher semantic relatedness in RC than UC (5 for highly related, RC 4.03 ± 0.02, UC 1.41 ± 0.02, t (383) = 85.02, p < .001). In the experiment, related and unrelated prime–target pairings were counterbalanced across all participants, stimulation levels (TMS vs. Baseline), and regions (LMTG vs. Vertex, or aLIFG vs. Vertex), with no difference in terms of psycholinguistic properties of the stimuli across sessions. After counterbalancing, no repeated word pairs were presented in the same session to any subject.

Following the timing of a previous study (Gold et al., 2006) which used short SOA (study 2) and long SOA (study 3) separately to emphasize early and late stages of word recognition, we also employed a short SOA of 150 ms and a long SOA of 600 ms. Following previous studies (Matsumoto et al., 2005; Rissman, Eliassen, & Blumstein, 2003), we used 600 ms as long SOA to ensure that stimuli would be presented within an appropriate time frame for TMS.

A schematic is shown in Fig. 1A. After a 300 ms fixation cross and subsequent 200 ms blank, the prime was visually presented either 150 ms or 600 ms depending on the SOA block, followed by the target presentation. Participants were asked to make a lexical decision to indicate whether or not the second word (target) was a real word within 2000 ms. Response terminated the target presentation, followed by a 200 ms blank. The inter-trial interval (ITI) was roughly 3 s. In each session there were 150 ms SOA and 600 ms SOA blocks. In each SOA block, there were 24 RC and 24 UC word pairs. In addition, 60 additional filler word pairs were

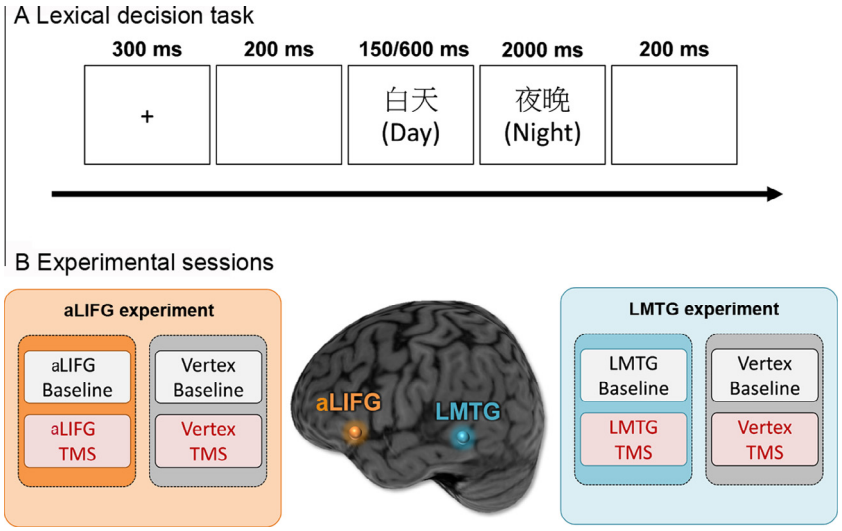

Fig. 1. Paradigm schematic. (A) The lexical decision task procedure was illustrated. (B) Experimental sessions. For each experiment, there was a critical stimulation site (aLIFG/LMTG) and a control site (Vertex). For each site, there were sessions with and without TMS (TMS vs. Baseline). In each day, the participant completed one site with one TMS session and one Baseline session. The order was counterbalanced between stimulated site (aLIFG vs. Vertex or LMTG vs. Vertex) and between TMS and Baseline session.

included with nonword targets to enable the lexical decision task. The aim of employing relative unbalanced number of word and nonword target was to limit random selection strategy, which was more useful when the number of word and nonword was equal. In each block, RC, UC and filler trials were pseudorandomly presented. Each participant received 4 practice trials prior to starting the task. All stimuli were presented using E-Prime software version 1.1. To better regulate timing of stimuli presentation, we used a CRT screen and prerelease function of E-Prime.

2.3. TMS protocol

The stimulation location was determined based on previous fMRI findings (Gold et al., 2006, experiment 3) that used semantic priming task and found significant activation in the aLIFG (Talairach–Tournoux coordinate, $x = -46$, $y = 33$, $z = -3$) and LMTG ($x = -55$, $y = -43$, $z = -1$). T1-weighted anatomical images were used to target the selected areas and stimulation sites were determined in native space. Brainsight Software (Rogue Research, Montreal, Quebec, Canada) was used to determine correspondence between the location at the skull and the site of stimulation on the scan. The Vertex was defined as position Cz according to the international 10–20-system for EEG.

In the present study, continuous theta-burst TMS was adopted (Huang et al., 2005). In this protocol 3 pulses were given at 50 Hz and were repeated every 200 ms for a total of 300 pulses in 20 s by a Magstim Super-Rapid stimulator (Whitland, Wales, United Kingdom). The same protocol has been used to effectively investigate higher cognitive functions in the human brain such as visual orienting (Chang et al., 2013; Liu et al., 2011) and object perception (Kim, Biederman, & Juan, 2011). This protocol has also been effectively used to disrupt language production through stimulation of left lateral prefrontal cortex (Nardone et al., 2011).

A Magstim Super-Rapid Stimulator with a 55-mm figure-of-8 coil was used to administer the TMS (300 pulses for each participant session). In each stimulation session, the TMS was administered once. Stimulation was set at 40% of the stimulator output for all participants based on past studies showing reliable TMS effects across a wide range of tasks (Chang et al., 2013; Kim et al., 2011; Liu et al., 2011) and because motor cortex excitability does not provide a good guide to TMS thresholds in other cortical regions (Stewart, Walsh, & Rothwell, 2001). During TMS over aLIFG and LMTG, the coil handle was oriented toward the superior portion of the head, and during stimulation over the Vertex, the coil handle was oriented toward the left side of the head. No uncomfortable effect was reported in the present study.

2.4. Procedure

In both the aLIFG experiment and LMTG experiment, we used a full factorial TMS vs. Baseline and aLIFG/LMTG vs. Vertex design with four combinations (hence four sessions) for each participant (see Fig. 1B). For the aLIFG experiment, the four sessions were aLIFG (Stimulation vs. Baseline) and Vertex (Stimulation vs. Baseline). For the LMTG experiment, the four sessions were LMTG (Stimulation vs. Baseline) and Vertex (Stimulation vs. Baseline). The participants completed a single site stimulation per day (aLIFG or Vertex in aLIFG experiment, LMTG or Vertex in LMTG experiment), with the order between Baseline measures, TMS, and location counterbalanced across participants. In the TMS session, the task was started 5 min after TMS to cumulate the TMS effect. The Baseline session was set to compare the TMS effect. Therefore, no TMS was used in this session. Moreover, the Baseline session was assessed before or after TMS in the same day, to build a more comparable baseline. If the TMS was administered before Baseline session, then a 1-h rest interval was implemented in order to prevent carry-over TMS effect. The length of the experiment was shorter than 15 min in each session, well within continuous theta burst stimulation effective time range. Furthermore, to avoid carry-over effect, 5–7 days intervals between stimulation on different sites (i.e. aLIFG vs. Vertex or LMTG vs. Vertex) were applied.

2.5. Data analysis

Data were analyzed using SPSS 18.0 for windows. At the first step, to identify the TMS effect and possible interactions between TMS and other factors, data analyses were performed for each task separately within each aLIFG and LMTG experiment. To overcome confounding effects, such as session order effect, learning or fatigue effects, we used linear mixed models (Baayen, Davidson, & Bates, 2008), a model widely used in linguistic literature. In the linear mixed model design, accuracy and RT of correct trials were set as dependent variables, SOA (150 ms vs. 600 ms), region (aLIFG vs. Vertex or LMTG vs. Vertex), relatedness (RC vs. UC), and TMS (Baseline

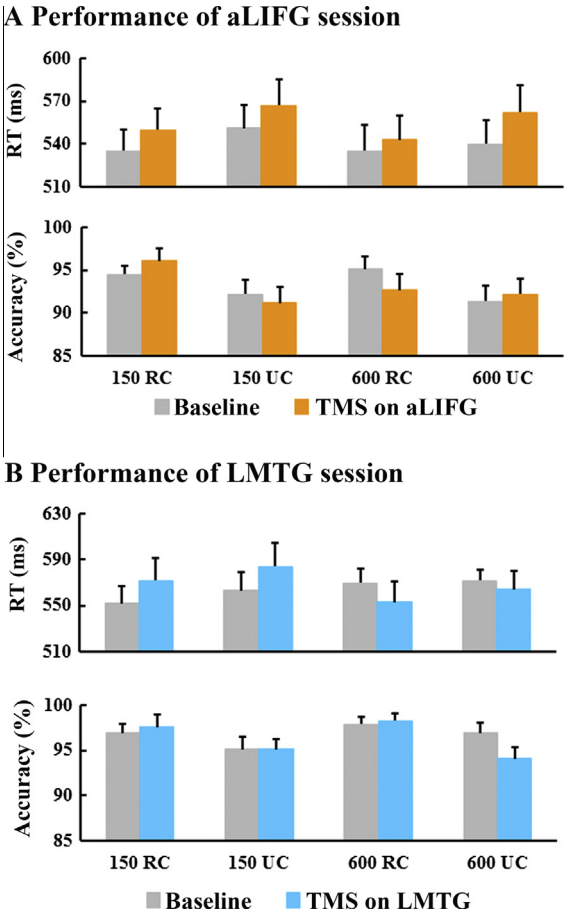

Fig. 2. Behavioral performance of aLIFG and LMTG session. (A) Performance of baseline and when aLIFG was stimulated. (B) Performance of baseline and when LMTG was stimulated.

Table 1
Accuracy and RT of Vertex in aLIFG experiment (mean ± standard error).

SOA (ms)	Relatedness	Vertex accuracy (%)		Vertex RT (ms)	
		Baseline	TMS	Baseline	TMS
150	Related	95.8 ± 1.2	95.3 ± 1.1	542 ± 15	540 ± 17
	Unrelated	93.5 ± 1.3	91.2 ± 1.6	549 ± 14	553 ± 18
600	Related	92.7 ± 1.6	95.6 ± 1.5	542 ± 19	550 ± 25
	Unrelated	93.2 ± 1.7	92.2 ± 2.3	557 ± 20	560 ± 23

vs. TMS) were set as fixed factors, and subject, item, session and presenting order were set as random factors. Trials in which RT was longer or shorter than 3 standard deviations were removed prior to RT analysis (0.5% for the aLIFG experiment, 0.45% for the LMTG experiment).

In the second step, to statistically test whether the aLIFG and LMTG contribute to a specific word recognition component, the accuracy and RT in the aLIFG and LMTG studies (but not Vertex) was combined in a linear mixed model for LDT. In the linear mixed model design, region (aLIFG vs. LMTG) was set as between subject factor, with SOA (150 ms vs. 600 ms), relatedness (RC vs. UC), and TMS (Baseline vs. TMS) were set as fixed factors, and subject, item, session and presenting order were set as random factors. Simple main effects were tested when significant interactions were observed, and post hoc tests were performed when significant main effects were observed. The numerator and denominator *df* (observation data points) were also presented in statistical results. The effect size was calculated via the partial eta squared (η^2) in SPSS, which is defined as the ratio of variance accounted for by an effect relative to the variance of that effect plus its associated error variance within an ANOVA.

3. Results

3.1. aLIFG experiment

Fig. 2A presents the performance results in the aLIFG session and Table 1 presents those in Vertex session in the aLIFG experiment. There was a main effect of both accuracy and RT for relatedness in the LDT. Specifically, participants showed higher accuracy rates for the RC when compared to the UC [94.7% vs. 92.1%, F (1,6125) = 17.10, p < .001, η^2 = 0.43], while also taking less time to respond for the RC when compared to the UC [542 ms vs. 555 ms, F (1,5647) = 21.80, p < .001, η^2 = 0.38]. There was also a significant main effect of TMS for RT with TMS resulting in increased RT compared to Baseline [544 ms vs. 553 ms, F (1,5647) = 21.80, p < .001, η^2 = 0.27]. We also observed significant SOA × Region interaction [F (1,5647) = 4.63, p = .031, η^2 = 0.10] and marginally significant TMS × Region interaction [F (1,5647) = 3.53, p = .06, η^2 = 0.07] for RT. No other significant effects were found (p-values >.25) on accuracy or RT. Thus, further analyses were performed in the aLIFG and Vertex separately to test the TMS effect on RT.

For aLIFG, TMS interference effect was observed, as RT in Baseline was shorter compared to RT following TMS [540 ms vs. 556 ms, F (1,2818) = 13.61, p < .001, η^2 = 0.30]. There was also relatedness effect, as RT in RC was shorter compared to the UC [541 ms vs. 555 ms, F (1,2818) = 12.89, p < .001, η^2 = 0.46]. No other effects on RT were significant (p-values >.18). For Vertex, RT for the 150 ms SOA was shorter than that for the 600 ms SOA [546 ms vs. 552 ms, F (1,2818) = 3.16, p = .043, η^2 = 0.05], and RT for the RC was shorter than RT for the UC [543 ms vs. 555 ms, F (1,2818) = 9.35, p = .002, η^2 = 0.25]. No other effects on RT were significant (p-values >.35).

3.2. LMTG experiment

Fig. 2B presents the performance results in the LMTG session and Table 2 presents those in the Vertex session in LMTG experiment. There was higher accuracy in the RC than UC [97.4% vs. 95.1%, F (1,4346) = 19.0, p < .001, η^2 = 0.46], but no other significant effects on accuracy (p-values >.15). The RT of the RC was also shorter than that of the UC [564 ms vs. 575 ms, F (1,4346) = 14.32, p < .001, η^2 = 0.35], RT in LMTG was shorter than that of Vertex [566 ms vs. 572 ms, F (1,4346) = 14.32, p < .001, η^2 = 0.03]. Significant SOA × TMS interaction (F (1,4346) = 4.04, p = .044, η^2 = 0.17) and SOA × TMS × Region interaction (F (1,4346) = 12.48, p < .001, η^2 = 0.28) on RT were also observed, but no other significant effects (p-values >.12). Thus, further analyses were performed in the LMTG and Vertex separately to test TMS effect on RT.

For Vertex, only RT of the RC was shorter than that of UC [566 ms vs. 579 ms, F (1,2173) = 10.03, p = .002, η^2 = 0.36]. RT in 150 ms SOA was slightly shorter than that in 600 ms SOA (F (1,2173) = 2.76, p = .097, η^2 = 0.02], but no other significant effects were observed (p-values >.30). For LMTG, there was also SOA × TMS interaction (F (1,2173) = 16.17, p < .001, η^2 = 0.41). In 150 ms SOA, RT following TMS was longer than that in Baseline (578 ms vs. 558 ms, p < .001, η^2 = 0.41). In 600 ms SOA, RT following TMS was shorter than that in Baseline (559 ms vs. 571 ms, p = .024, η^2 = 0.18). And generally, RT in the RC was shorter than that in the UC [561 ms vs. 571 ms, F (1,2173) = 4.51, p = .034, η^2 = 0.20] in LMTG. No other significant effects were observed (p-values >.39).

Table 2
Accuracy and RT of Vertex in LMTG experiment (mean ± standard error).

SOA (ms)	Relatedness	Vertex accuracy (%)		Vertex RT (ms)	
		Baseline	TMS	Baseline	TMS
150	Related	97.2 ± 1.2	97.9 ± 1.2	565 ± 18	560 ± 13
	Unrelated	96.5 ± 1.2	94.1 ± 1.8	581 ± 21	568 ± 17
600	Related	96.2 ± 1.3	97.2 ± 0.9	569 ± 18	569 ± 14
	Unrelated	94.4 ± 1.6	94.4 ± 1.6	583 ± 17	583 ± 14

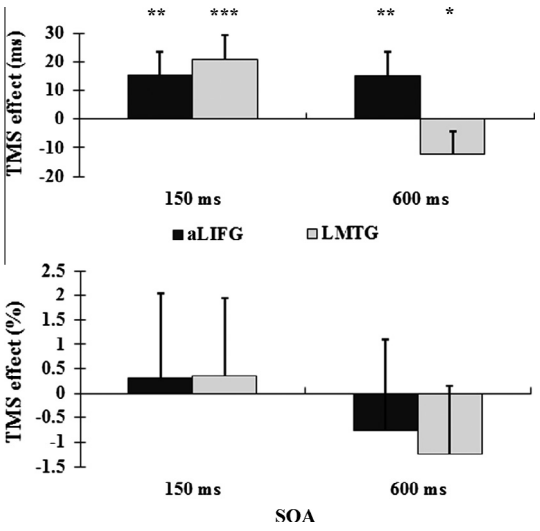

Fig. 3. TMS effect in aLIFG and LMTG for each SOA. In the top panel, TMS effects on RT were presented. In the bottom panel, TMS effects on error rate were presented. Note: Asterisk indicates significant TMS effect (TMS vs. Baseline). $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

3.3. Result in combined analysis

In the combined analysis, the aim was to test the role of aLIFG and LMTG in word recognition. Specifically, we set region (aLIFG vs. LMTG) as between subject factor, and set TMS (Baseline vs. TMS), relatedness (RC vs. UC) and SOA (150 ms vs. 600 ms) as within subject factors to test whether there was any interaction involving relatedness. While a significant relatedness effect [$F(1,4992) = 15.81$, $p < .001$, $\eta^2 = 0.33$] was found, no significant interaction between relatedness and the other three factors was observed. To simplify the data presentation, we removed the relatedness in the following analysis. The averaged RT thus represented general word recognition speed.

Fig. 3 top panel presents the RT effect. When the aLIFG and LMTG studies were combined in linear mixed model analysis, there was a significant region effect [$F(1,3361) = 111.23$, $p < .001$, $\eta^2 = 0.28$] and TMS effect [$F(1,4992) = 9.61$, $p < .001$, $\eta^2 = 0.17$]. Importantly, we found that the TMS effect was modulated by region and SOA, evidenced by significant TMS × region interaction [$F(1,4992) = 3.96$, $p = .047$, $\eta^2 = 0.04$], TMS × SOA interaction [$F(1,4992) = 8.57$, $p = .004$, $\eta^2 = 0.12$] and TMS × region × SOA interaction [$F(1,4992) = 7.49$, $p = .007$, $\eta^2 = 0.12$], but no other significant effects (p-values >.18). For aLIFG, there was significant TMS interference effect in 150 ms SOA condition ($p = .004$, $\eta^2 = 0.32$) and 600 ms SOA condition ($p = .009$, $\eta^2 = 0.26$). For LMTG, significant TMS interference effect was found in 150 ms SOA condition ($p < .001$, $\eta^2 = 0.41$), while significant TMS facilitated effect was observed in 600 ms SOA condition ($p = .024$, $\eta^2 = 0.18$).

To test whether the TMS effect on RT is due to accuracy-RT tradeoff, the accuracy TMS effect was tested though no TMS effect was found in previous analyses. No significant TMS effect was found in any condition, as shown in bottom panel in Fig. 3 (p-values >.30).

4. Discussion

By comparing lexical decision task (LDT) performance at Baseline and after TMS stimulation, we tested whether aLIFG and LMTG regions are necessary for speeded word recognition. We observed a region × TMS interaction such that RT was more affected by aLIFG or LMTG stimulation than TMS to a control region (Vertex). Furthermore, we manipulated short and long SOA between prime and target to clarify whether the aLIFG and LMTG may play different roles during lexical processing.

Previous research has suggested roles for both aLIFG and LMTG in explicit semantic processing (Badre et al., 2005; Giesbrecht et al., 2004). However, the role of these regions in word recognition is less clear. The absence of aLIFG and LMTG activation in some functional neuroimaging studies raises the possibility that these regions may not make significant contributions to lexical processing in the absence of explicit semantic decision. Similarly, whereas neuropsychological studies have generally found that lesions in and around peri-Sylvian regions impaired word recognition performance (Dronkers et al., 2004; Hagoort, 1993; Milberg & Blumstein, 1981; Swick, 1998), focal lesions to aLIFG or LMTG are rare.

Convergent evidence from TMS would therefore be helpful in understanding the relevance of aLIFG and LMTG in lexical processing. Comparison of TMS interference with Baseline revealed medium to large effect sizes according to published criteria (Cohen, 1988). These effect sizes support a view that aLIFG and LMTG are critically involved in word recognition speed. Compared to TMS of a control region, stimulation of aLIFG or LMTG significantly affected lexical decision RT. These results provide convergent TMS evidence in support of some previous functional neuroimaging studies (Bookheimer et al., 1995; Heim et al., 2009; Madden et al., 2002) and some neuropsychological data (Swick, 1998), suggesting roles for aLIFG and LMTG in word recognition.

A second aim was to address the possibility that aLIFG and LMTG may play different roles during lexical processing. Automatic and controlled components of the lexical system have been appreciated at the behavioral level for several decades (Neely, 1977; Neely, Keefe, & Ross, 1989). The automatic component occurs within a few hundred milliseconds following word presentation guides rapid, implicit access to lexical representations. In contrast, the controlled component evolves more slowly and allows for strategic, efficient retrieval of lexical representations not recovered automatically. Our results suggest that aLIFG and LMTG may play similar roles during early components of lexical processing but may play different roles during later stages of word recognition. At short SOA, TMS of the aLIFG and the LMTG regions had similar effects, in each case prolonging RT. With respect to LMTG, our results cross-validate previous functional neuroimaging findings that have suggested a role for this region in early stages of visual word recognition (Devlin et al., 2004; Gold & Rastle, 2007; Gold et al., 2006; Lau et al., 2008; Sass et al., 2009; Wheatley et al., 2005). As for aLIFG, our findings are consistent with evidence from previous MEG studies reporting that aLIFG is involved in early stages of word recognition, being activated within the first 185 ms or so of word presentation (Cornelissen et al., 2009; Dale et al., 2000; Shtyrov & Pulvermuller, 2007; Woodhead et al., 2014).

Our results that TMS of aLIFG at long SOA served to prolong lexical decision RT is consistent with functional brain imaging studies that have reported activation in this region associated with strategic verbal processing (Badre et al., 2005; Gold et al., 2006). The

observation that LMTG stimulation also affected lexical decision RT is consistent with results from some previous fMRI studies suggesting that LMTG may also contribute to strategic in addition to more automatic word recognition processes (Gold et al., 2006).

However, TMS suppression of LMTG at long SOA actually facilitated LDT-RT. This was an unexpected finding. The speeding of RT associated with TMS of LMTG, in the absence of effects on accuracy, suggests that LMTG may play a role in a controlled strategy which is not strictly necessary for accurate lexical decision. One such strategy is the post-lexical semantic matching strategy (de Groot, 1984; Neely et al., 1989) in which the reader may check for a semantic relationship between the target and the prime to guide their LD (Balota et al., 1992; Neely, 1991) when there is enough time to generate strategies, i.e. in long SOA condition. TMS of LMTG may disrupt the semantic matching process at long SOA, which could speed RT. The notion that LMTG contributes to a semantic matching process is in line with results from another TMS study in which semantic matching constituted the task itself and was thus required for accurate task decision (Whitney, Kirk, O'Sullivan, Lambon Ralph, & Jefferies, 2011).

Interestingly, we did not find interactions between TMS and semantic prime–target relatedness. One possible reason for the null effect could be that aLIFG and TMS do not contribute to semantic components of word recognition. However, there is considerable evidence that these regions do contribute to semantic components of word recognition (reviewed in Lau et al. (2008)). A different possibility is that, since semantic priming effects are relatively small, they can be maintained by other portions of the fronto-temporal network. There is broad support for this view (Gold et al., 2006; Gough, Nobre, & Devlin, 2005; Wu, Ho, & Chen, 2012). For example, a number of other regions have been linked with semantic components of word recognition such as anterior or middle portions of the fusiform gyrus (Gold et al., 2006), anterior middle temporal gyrus (Rossell et al., 2003), the temporal pole (Hodges, Patterson, Oxbury, & Funnell, 1992; Nobre, Allison, & McCarthy, 1994). It appears that interfering with aLIFG and LMTG functioning is insufficient to disrupt semantic priming effects.

We note several caveats of the present study. First of all, our TMS effects were relatively small. The small TMS effects could relate to several factors, such as relatively low trial numbers per condition, potential compensation from brain regions that are the highly connected to, and interact with, the TMS disrupted region, relative weak statistical power due to limited sample size, a fixed TMS output without adjusting distance effect (distance between site and motor cortex) (Stokes et al., 2013), or TMS effects that were less localized than expected. Second, we note that the use of semantic primes in our study may have encouraged subjects to emphasize semantic processes relative to phonological or orthographic processes during lexical decisions, an issue that should be explored in future studies. Furthermore, to limit the stimulation times and potential practice and/or learning effects on the stimuli, we recruited different subjects for the aLIFG and LMTG studies. Future studies in this area should attempt to apply TMS to different brain regions of a single group of subjects, while still controlling for practice and learning effects to avoid potential pre-existing differences between subjects. As different types of orthographic scripts may influence the relative engagement of linguistic sub-systems (Tan, Laird, Li, & Fox, 2005), future research should assess the generalizability of our TMS findings to lexical decisions performed on alphabetic scripts such as English. Finally, as aLIFG and LMTG have been associated with multiple functions, it would be interesting to test whether TMS on these regions also disrupt other cognitive function in future studies.

In summary, the present study provides evidence that both the aLIFG and LMTG make causal contributions to the lexical decision speed. Our results also provide preliminary evidence suggesting that the aLIFG and the LMTG appear to play more similar roles during early stages of word recognition than they do at later stages. Finally, our results suggest that semantic priming effects are likely to be subserved by a distributed brain network beyond the aLIFG and LMTG.

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