Broca's area plays a causal role in morphosyntactic processing

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Although there is strong evidence that Broca's area is important for syntax, this may simply be a by-product of greater working memory and/or cognitive control demands for more complex syntactic structures. Here we report an experiment with event-related transcranial magnetic stimulation (TMS) to investigate whether Broca's area plays a causal role in morphosyntactic processing when both working memory and cognitive control demands are low. Participants were presented with word pairs that could either agree or disagree in grammatical number or gender while receiving stimulation to Broca's area or to the right intraparietal sulcus (a control site). Stimulation of Broca's area significantly reduced the advantage for grammatical relative to ungrammatical word pairs. In contrast, stimulation of control site left this grammaticality advantage unchanged. The interaction between grammaticality and stimulation was specific to Broca's area, suggesting a clear involvement of the region in morphosyntactic processing.

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1. Introduction

Broca's area is an important hub for language processing, however, its specific role is still unclear and under ongoing debate (see Rogalsky & Hickok, 2011). In the sixties it was conceptualized as the syntactic core for comprehension and production processes taking into account the performance of the so-called Broca's aphasics (Bradley, Garret & Zurif, 1980; Caramazza & Zurif, 1976; Gleason, Goodglass, Green, Ackerman, & Hyde, 1975; Goodglass, 1968, 1976; Goodglass & Berko, 1960; Goodglass & Kaplan, 1972; Kean, 1977, 1995). However, this view was challenged when it was discovered that a) Broca's aphasics were able to make syntactic judgments (Linebarger, 1990; Linebarger, Schwartz, & Saffran, 1983; Martin, 2003; Wulfeck, 1988), and b) the relationship between Broca's aphasia and damage to Broca's area was not so simple, revealing a very complex relationship between the behavioral deficit and the anatomy. In fact, it has been reported that damage to Broca's area alone does not necessarily result in Broca's aphasia (Mohr et al., 1978).

Evidence from functional neuroimaging studies added fuel to the debate, but did not help to settle it. Many fMRI studies, using different tasks, stimuli, languages, and paradigms have found activation of left inferior frontal areas during syntactic processing (e.g., Indefrey, Hagoort, Herzog, Seitz, & Brown, 2001; Indefrey et al., 2004). In particular, some experiments showed that activity in Broca's area was greater during the comprehension of complex structures (Caplan, Alpert, & Waters, 1998; Caplan, Alpert, & Waters, 1999; Dapretto & Bookheimer, 1999; Just, Carpenter, Keller, Eddy, & Thulborn, 1996; Stromswold, Caplan, Alpert, & Rauch, 1996) and in particular when manipulating syntactic complexity, such was when comparing long versus short distance movement dependencies (Cooke et al., 2002; Fiebach, Schlesewsky, Lohmann, von Cranom, & Friederici, 2005; Grodzinsky & Santi, 2008; Grodzinsky, 1986, 2000; Rogalsky, Matchin, & Hickok, 2008; Santi & Grodzinsky, 2007a,b). However, long distance movement dependencies involve heavier working memory load. Thus, the greater activity in Broca's area attributed to the movement distance effect could be just triggered by domain-general working memory load (Just et al., 1996; King & Just, 1991; Rogalsky et al., 2008). In fact, it is known that Broca's area is activated in verbal working memory tasks (Awh et al., 1996; Buchsbaum & D'Esposito, 2008; Buchsbaum, Olsen, Koch, & Berman, 2005; Hickok, Buchsbaum, Humphries, & Muftuler, 2003; Smith & Jonides, 1997; Smith, Jonides, & Koepp, 1996).

Broca's area has also been suggested to be involved in cognitive control and conflict monitoring (Duncan & Owen, 2000). Although both functions are critical for language processing, neither is
specific to a linguistic context. For instance, when patients with lesions to Broca’s are faced with conflicting information between competing representations their performance is impaired in both lexical and non-lexical tasks (Novick, Trueswell, & Thompson-Schill, 2005). Similarly, functional neuroimaging studies demonstrate that Broca’s area responds equally strongly to lexical and non-lexical conflict (Simard et al., 2011; Ali, Green, Kerif, Devlin, & Price, 2010). Thus, increased cognitive control processes linked to more complex sentences might also explain Broca’s area involvement associated with syntactic processing.

Finally, other studies provided evidence on the critical role played by the left inferior frontal gyrus in processing morphosyntactic information. Morphosyntactic anomalies between subject and verb number agreement produced an enhanced activation in the inferior frontal gyrus (Ni et al., 2000; Newman, Just, Keller, Roth, & Carpenter, 2003). Gender features also seem to activate a network that involves the inferior frontal gyrus. Miceli et al. (2002) found an increase of activation in the left middle and inferior frontal gyrus when participants were presented with a written noun and responded whether its grammatical gender was masculine or feminine. Hernandez et al. (2004) found increased activity in the left inferior frontal gyrus during the processing of words with opaque gender as compared to those with transparent gender in Spanish. They suggested that the gender decision for opaque words required additional morphological processing than that for transparent words. In addition, a recent study provided consistent evidence for the involvement of the inferior frontal gyrus during the processing of grammatical gender and number agreement in Spanish (Carreiras et al., 2010). They investigated the processing of number and gender agreement anomalies between determiner-noun and adjective-noun pairs. Both gender and number anomalies were found to produce increased activation in the left inferior frontal and left premotor regions. Thus, the purely grammatical effects common to the two disagreement conditions led to the common increase of activation in left frontal and pre-motor regions.

Thus, there is considerable debate regarding the role of Broca’s area in syntactic processing. Although there is strong evidence that the region is important for syntax, this may simply be a by-product of greater working memory and/or cognitive control demands for more complex syntactic structures. Here we report an experiment with event-related transcranial magnetic stimulation (TMS) to clarify the role of Broca’s area. In particular we investigated whether it plays a specific role in morphosyntactic processing when both working memory and cognitive control demands are minimal. To that end we visually presented determiner-noun pairs and asked participants to indicate whether the two words grammatically agreed. Using similar stimuli it was found that both gender and number violations modulated the LAN and the P600 in an event related potentials experiment (Barber & Carreiras, 2005) and that both violations produced increased activation in the left inferior frontal and left premotor regions relative to the agreement condition (Carreiras et al., 2010). These studies demonstrate that the paradigm strongly engages Broca’s area and indicate its role in syntactic processing. However, one cannot infer that the role is causal without perturbing its function and observing a change in behavior. Consequently, if the region causally contributes to morphosyntactic processing, we should be able to selectively modulate reaction times when TMS is administered to Broca’s area but not when administered to a control site.

2. Methods

2.1. Participants

Twelve right-handed, native Spanish speaking volunteers (8 women; age ranged from 19 to 41) participated in the study. Each participant received 20 GBP for participating. Participants were assessed for handedness with an abridged Spanish version of the Edinburgh Handedness Inventory (Oldfield, 1971). None had any form of dyslexia, a personal history of neurological disease, or a family history of epilepsy according to self-reports. Each gave informed consent after the experimental procedures were explained. The experiments were approved by the Berkshire NHS Research Ethics Committee (06/Q1602/20).

2.2. Design

Participants performed a grammaticality judgement task where Spanish determiner-noun pairs were visually presented on a computer screen. Participants decided whether the pair was grammatically correct or not, indicating their response with a button press. Whether Broca’s area is involved in this type of grammatical processing was tested using a simple 2 × 2 design where Agreement (grammatical vs. violation) and TMS (stimulation vs. no stimulation) were the two independent factors. A TMS × Agreement interaction would demonstrate that stimulation of Broca’s area affects performance, indicating its involvement in grammatical processing. Although it is possible that a main effect of TMS might also indicate Broca’s area involvement, it could just as easily be a non-specific artefact of stimulation due to the unusual sensation of TMS. Consequently, an additional control site was tested to rule-out non-specific stimulation effects.

2.3. Procedure

Testing began by collecting a single T1-weighted MRI scan per participant so that Broca’s area (and the control site) could be anatomically localized and individually targeted in each participant. Whole brain imaging was performed on a Siemens 1.5-Tesla MRI scanner at the Birkbeck-UCL Centre for Neuroimaging (BUCNI) in London. A high-resolution anatomical scan was acquired (T1-weighted FLASH, TR = 12 ms, TE = 5.6 ms, 1 mm² resolution) that included fiducial landmarks for co-registering the image to the individual’s head using a frameless stereotaxic system (Brainsight, Rogue Research, Montreal, Canada). The specific site within Broca’s area was marked as the crest of left pars opercularis approximately 1 cm below the inferior frontal sulcus. On average, the standard space (i.e. MNI152) coordinate for this was (−58, 12, 22), a site within pars opercularis corresponding to Brodmann’s area 44 (Amunts et al., 1999).

Because the effects of TMS can spread trans-synaptically (Paus et al., 1997; Siebner, Hartwigsen, Kassuba, & Rothwell, 2009; Valero-Cabre, Payne, Rushmore, Lomber, & Pascual-Leone, 2005), it was important to choose a control site without direct cortico-cortical connections linking it to pars opercularis in particular or Broca’s area more generally. We chose the depth of the right intraparietal sulcus (IPS) as a control site in part because it is not typically implicated in grammatical (or even language) processing nor is it directly connected to such regions (which tend to be left-hemisphere dominant). In addition, IPS stimulation produced a mild enervation of the temporo-parietal muscle, albeit not as pronounced as Broca’s area stimulation. Nonetheless, the sensation was more comparable than using vertex and thus was a better control for non-specific effects of stimulation. The mean standard space coordinate across participants was (+40, −48, 40). Both Broca’s area and the IPS control site were tested in a single TMS session that occurred at least 24 h after acquiring the structural scan.

The TMS session started with an opportunity for participants to practice the grammaticality judgement task. Each trial began with a “+” presented for 500 ms to visually cue the participant. This was followed by a determiner (el, la, or los) for 300 ms then a blank screen for 200 ms and a second word (a noun) for 300 ms. Finally a blank screen was presented for an additional 1800 ms (see Fig. 1). The word pair either agreed in both gender and number (e.g. el piano) or disagreed in either gender (e.g. la piano) or number (e.g. los pianos). Participants were instructed to judge whether the trial was grammatically congruent, that is, whether or not the
two words agreed in both gender and number. They pressed one button to indicate a trial was grammatically correct and other if it was incorrect. The assignment of hands was counterbalanced across participants. Accuracy and reaction times were recorded.

After practicing the task, participants were introduced to the sensation of TMS at the first testing site (either Broca’s area or right intraparietal sulcus—the order of sites was counterbalanced across participants). Then they practiced the task again with this time with stimulation delivered pseudorandomly on half of the trials to become acclimated to performing the task during stimulation. Pulses were delivered at 10 Hz for 500 ms (i.e. at 0, 100, 200, 300, and 400 ms post target onset) – that is, starting with the presentation of the noun. The intensity of the repetitive TMS (rTMS) was set to 45% of maximum stimulator output for Broca’s area and 60% of maximum output for right intraparietal sulcus. The different intensities reflect the different depths of the stimulation locations. Because the opercularis site was situated on the crest of the gyrus, the average distance from the coil to the site was 19.3 mm. In contrast, the right IPS site was located at the fundus of the sulcus with an average depth of 31.4 mm. Consequently, we adjusted the intensity to attempt to account for this discrepancy (Stokes et al., 2005, 2007). The same stimulation intensities were used for all participants. The choice of intensities was based on similar experiments in which the common choice was 60% of the maximum stimulator intensity when using 10Hz stimulation (Gough, Nomura, & Devlin, 2005; Pitcher, Walsh, Yovel, & Duchaine, 2007; Sack et al., 2009; Silvanto et al., 2010). A Magstim Rapid2™ stimulator (Magstim, Whitland, UK) with a 70-mm figure-of-eight coil was used to deliver the stimulation. None of the stimuli used in the practice sessions occurred in the main task.

The main experiment consisted of two separate testing blocks within a single session. The first testing site stimulation was the same as the practice site. At that site, participants performed a single block of the task consisting of 128 pseudorandomly ordered trials, half of which were grammatically correct. rTMS occurred on half of the trials, evenly distributed between grammatical and ungrammatical trials. The second block of trials was essentially identical, except that stimulation was delivered to the other site. There was approximately a 5 min break between blocks. In total, a TMS session lasted approximately 1 h.

2.4. Stimuli

In Spanish it is mandatory that determiners, nouns and adjectives agree in gender and number. In the present experimental stimuli, gender was always a strictly morphosyntactic feature without semantic significance. All nouns and adjectives were morphologically marked in gender and number, this is, they ended with the canonical suffixes in Spanish for gender (“-o” for masculine and “-a” for feminine) and number (“-s” or “-es” for plural). This way, both gender and number agreement were similar in terms of transparency cues for agreement. Although there are some exceptions (e.g. “tEsis” [thesis]) in which ending does not change for singular and plural, number is almost always transparent, while gender is not. All nouns were of monosyllabic frequency according to the Spanish database (Sebastián, Martí, Carreiras, & Cueto, 2000) and of 3–7 letters long.

The full set of stimuli consisted of 256 determiner-noun word pairs, divided into two equal lists that were counterbalanced across testing sites. Within a list, 64 items were grammatically correct and half of these used morphologically opaque nouns where the gender was not identifiable by looking at the word ending such as the word “tejoy” [clock] which lacks any explicit morphological marking or irregular words like “mamo” [hand] which ends with the letter “-o” but is feminine. Consequently, this prevented participants from using a superficial strategy for solving the task such as, for example, attending to the letters. The remaining 64 trials were grammatically mismatched in gender or number, such that participants had to respond yes and no the same number of times. Each participant received a different randomization order of the trials.

3. Results

Accuracy and reaction times are displayed in Fig. 2. The overall accuracy rate was 92% indicating that participants had no difficulty performing the task. Accuracy scores were analysed with a repeated-measures 2 × 2 ANOVA with Agreement (grammatical, ungrammatical) and TMS (absent, present) as independent factors.

1 By adding an additional control site (IPS), the experiment could be considered as a 2 × 2 × 2 design with Agreement, TMS, and Site as independent factors. However, given a small sample size in our study (n = 12), there was insufficient statistical power for the 3-way interaction to reach significance. Although it was possible to test additional participants, there is a potential ethical issue to weight against our desire for greater statistical rigor. Namely, there is a small, but non-zero, risk associated with TMS even in healthy individuals who are properly safety-screened. The most important point here is that the full 2 × 2 × 2 design proved unnecessary in the present study for two reasons. First, we observed a significant Agreement × TMS interaction for Broca’s area stimulation, i.e., stimulation selectively affected the grammatically incompatible trials and not those that had grammatical agreement – a finding that is very difficult to explain in terms of a non-specific effect of TMS. Second, the patterns of results across the two regions were clearly qualitatively different which further confirmed that the effect observed on Broca’s area could not be due to non-specific TMS effects.

There were no reliable main effects but the Agreement × TMS interaction was significant (F(1, 11) = 5.33, p = 0.040) due to the high accuracy score for grammatical items without TMS (97%).

In the analysis of reaction times, incorrect responses and reaction times above or below 1.5 standard deviations (11% of the word data equally distributed in the different conditions) were excluded from the latency analyses. There was a significant main effect (interaction (F(1, 11) = 42.15, p < 0.001) indicating that responses were faster when the word pairs were grammatical relative to ungrammatical (716 vs. 786 ms). There was no main effect of TMS (F(1, 11) = 0.39, n.s.) but there was a significant interaction (F(1, 11) = 4.88, p < 0.05) indicating that stimulation affected grammatical and ungrammatical trials differently. Indeed, from Fig. 1 it is apparent that stimulation to Broca’s area reduced the agreement effect – that is, the difference in reaction times between ungrammatical and grammatical pairs. Although this effect was present both for trials with (49 ms) and without TMS (89 ms), the magnitude of the effect was significantly reduced during TMS. This reduction was driven by a non-significant facilitation for ungrammatical trials where response times were an average of 33 ms faster with TMS than without it (t(11) = 1.6, p = 0.13).

The accuracy and reaction time data from the control site (the right intraparietal sulcus) were analysed in an equivalent manner to determine whether the TMS effects were specific to Broca’s area. The data are shown in Fig. 3. As before, the overall accuracy rate was 92% but stimulation to the control site produced no significant main effects of Agreement (F(1, 11) = 0.4, n.s.) nor TMS (F(1, 11) = 0.4, n.s.)
on accuracy, and unlike Broca’s area, stimulation did not interact with accuracy ($F(1,11)=0.8$, n.s.). Instead, accuracy for all four conditions was very similar (89–93%) suggesting that the interaction in Broca’s area may have been driven by the atypically high accuracy score for grammatical pairs without TMS (97%) rather than a true effect of TMS.

In the analysis of reaction times, once again there was a main effect of Agreement on reaction times ($F(1,11)=6.38, p<0.001$) but no effect of TMS ($F(1,11)=0.07$, n.s.) nor a significant interaction ($F(1,11)=0.21$, n.s.). The agreement effects of 36 and 23 ms, with and without TMS, were statistically equivalent. It is clear from the figure that stimulation had essentially no effect on either grammatical or ungrammatical trials ($F(1)<1$, n.s.). In other words, TMS to the right intraparietal sulcus affected neither accuracy nor reaction times, confirming the site’s appropriateness as a control location.

4. Discussion

The aim of this study was to investigate whether there is a causal relation between neuronal activity in Broca’s area and grammatical processing of determiner-noun pairs in Spanish. The present experiment shows that this is the case. Stimulation of Broca’s area significantly reduced the advantage for grammatical relative to ungrammatical word pairs from 89 to 49 ms. In contrast, stimulation of the intraparietal control site left this grammaticality advantage unchanged. In other words, the interaction between grammaticality and stimulation was specific to Broca’s area, suggesting a clear involvement of the region in morphosyntactic processing. These results agree with functional neuroimaging studies that have demonstrated that processing grammatical gender increases activation in Broca’s area (Carreiras et al., 2010; Hernandez et al., 2004; Miceli et al., 2002). In addition, this result is congruent with many other fMRI studies that have shown an increase of activation in Broca’s area by manipulating other features of syntactic processing (e.g. Fiebach et al., 2001, 2005; Friederici et al., 2003; Grodzinsky & Santi, 2008; Grodzinsky, 1980, 2006; Heim et al., 2002; Indefrey et al., 2001, 2004; Moro et al., 2001; Ni et al., 2000; Rogalsky et al., 2008; Santi & Grodzinsky, 2007, a, b).

More importantly, our results also indicate that Broca’s area has a causal link with syntactic processes, and therefore is also consistent with some previous TMS studies (Cattaneo, Devlin, Vecchi, & Silvanto, 2009; Sakai et al., 2002) but see Cappelletti et al. (2008). In particular, Sakai et al. (2002) contrasted sentences requiring syntactic decisions with sentences requiring semantic decisions and found syntactic (but not semantic) priming effects when TMS was administered to Broca’s area. Similarly, Cattaneo et al. (2009) found that stimulation of Broca’s facilitated access to “saturated” grammatical categories. That is, they used a satiation paradigm in which verbal repetition of a category name leads to a reduced access to that category. As expected, subjects were slower in responding to exemplars of the saturated category (either masculine or feminine) relative to exemplars of the nonsaturated category. Moreover, the application of TMS to Broca’s area removed the behavioral impact of the satiation and facilitated response times. All three studies converge that stimulation of Broca’s area facilitated syntactic processing, demonstrating a causal link.

It remains unclear, however, exactly how Broca’s area contributes to syntactic processing. Some authors have suggested the region supports sentence processing in a nonspecific way via its role in some form of general working memory (Just et al., 1996; Kaan & Swaab, 2002; Rogalsky et al., 2008) while others have argued that Broca’s area supports a syntactic-specific form of working memory (Fiebach et al., 2005). However, the task used in the current experiment does not seem to entail different working memory demands for the agreement and the violation condition. Thus our results would agree with the idea that Broca’s area may support more automatic syntactic processing that does not need to rely heavily on working memory processes. In the current experiment, TMS principally affected ungrammatical pairs that require integrating incompatible grammatical information. Indeed, Hagoort (2005) has argued that Broca’s area is involved in integrating linguistic information from phonological, semantic, and syntactic sources into a coherent representation of the utterance. In fact, according to the framework proposed by Hagoort (2005) an important function of Broca’s region is to integrate lexically retrieved information into a representation of multi-word utterances that entails computing syntactic and semantic relations between words. This operation of combining and integrating independent elements into a coherent overall representation necessarily involves checking agreement features such as gender and number between words, and this particular process was found to be modulated by TMS in the present experiment.

Thus results of our experiment converge with evidence from neuropsychological, neurophysiological, and neuroimaging studies in suggesting that morphosyntactic processing is represented in a network that includes Broca’s area. In addition, this current set of data critically demonstrates a causal role of Broca’s area in processing and integrating morphosyntactic information. Our findings, nonetheless, do not preclude the possibility that Broca’s area also plays a role in syntactic movement operations (Grodzinsky & Santi, 2008; Grodzinsky, 1986, 2000; Santi & Grodzinsky, 2007, a, b) or in a more general process underlying sentence processing (Just et al., 1996; Kaan & Swaab, 2002; Rogalsky et al., 2008) since the region is likely to participate in multiple functions. The current results, however, clearly demonstrate Broca’s area involvement in more automatic and local morphosyntactic integration operations.

More work is needed to understand the causal role of Broca’s area in syntactic processing. Functional disruption of Broca’s area and of the patterns of connectivity of networks that involve Broca’s area will help us to understand how functional anatomy gives rise to cognitive processing.

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