Role of Broca's area in encoding sequential human actions: a virtual lesion study

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The exact contribution of Broca's area to motor cognition is still controversial. Here we used repetitive transcranial magnetic stimulation (5 Hz, five pulses) to interfere transiently with the function of left BA44 in 13 healthy individuals; the task consisted of reordering human actions or nonbiological events based on three pictures presented on a computer screen and extracted from a video showing the entire sequence beforehand. We found that a virtual lesion of left BA44 impairs individual performance only for biological actions, and more specifically for object-oriented syntactic actions. Our finding provides evidence that Broca's area plays a crucial role in encoding complex human movements, a process which may be crucial for understanding and/or programming actions. ***NeuroReport*** **20:1496–1499 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

The contribution of Broca's area to processes other than language is now widely recognized as indicated by its possible involvement in some aspects of memory, calculation [1], and music processing [2]. Moreover, Broca's area is likely to contribute to high-level motor functions as suggested by the finding that some patients with lesions of the left inferior frontal gyrus may show apraxia [3]. Functional imaging studies have also reported activations of Broca's area during various motor-related paradigms such as observation [4], execution [5,6], imitation [7] of actions and during motor imagery [8].

Action observation is of particular interest because of the cytoarchitectonic similarity of Broca's area with monkey premotor area F5, where mirror neurons have been originally found [9] and because several neuroimaging studies have suggested that Broca's area may be critically involved in this process. For instance, it has been shown that the activation of Broca's area varied with the complexity of observed actions, indicating that this area could underlie the pragmatic encoding of observed actions in relation with their hierarchical organization [10]. Along the same lines, a recent study has revealed that patients with a lesion involving Broca's area present deficits in reordering pictures showing human actions, whereas this ability was preserved for nonbiological events [11]. This finding further supports the hypothesis that Broca's area could play a key role in encoding the hierarchical structure or, in other words, the motor syntax, of human actions. However, although patient studies provide useful cues about the causal relationship between the Broca's area lesion and the aforementioned behavioral deficits, the conclusions of such a study may be biased by the extent of the lesion and/or the possible brain reorganization, which may have occurred since that lesion.

To circumvent these limitations, we performed an interferential transcranial magnetic stimulation (TMS) experiment in healthy individuals, based on a paradigm close to that developed by Fazio and collaborators [11]. TMS was delivered over the pars opercularis of left Brodmann area (BA) 44, which corresponds to the posterior part of Broca's region, the site where the maximum overlap between patient's lesions was found by Fazio *et al.* [11].

Methods

Participants

Thirteen volunteers (mean age ± SD: 26.1 ± 5.4 years), right-handed as assessed by the Edinburgh handedness inventory [12], without any history of neurological disorders, participated in this experiment. They were screened for contraindications to TMS and informed about the nature of the experiment. All participants gave their written informed consent and were paid for their participation. rTMS was administered according to current safety guidelines [13] and all procedures used in this study were approved by the Ethics Committee of the Université Catholique de Louvain, in agreement with the Declaration of Helsinki.

Experimental procedure

The task consisted in reordering three pictures extracted from a video showing either a human action or a nonbiological event that is an object in movement (Table 1). We used the same 15 biological and 10 nonbiological videos as those used by Fazio and collaborators [11] and

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added five new nonbiological videos to reach the same number of biological and nonbiological videos. Each video was presented four times in four different blocks of 30 trials each (15 biological and 15 nonbiological trials pseudorandomly distributed). The experiment was run on a personal computer connected to a touch-sensitive screen and controlled by a custom-made program running under LabVIEW (National Instruments; Austin, Texas, USA). The time course of a trial is illustrated in Fig. 1. After showing the video, three pictures extracted from it were displayed simultaneously, in a random order, on the computer screen and participants had to point, with the right index finger, toward the picture representing the middle of the sequence. Participants were instructed to perform the task as accurately and as quickly as possible. The error rate and reaction time (RT, the delay between the onset of the three picture display and the moment when the finger touched the screen) were automatically recorded and stored for off-line analysis. Each experiment started with a practice block followed by the four experimental blocks (two per site of stimulation, counterbalanced across participants, see below).

Table 1 List the 15 biological and nonbiological videos

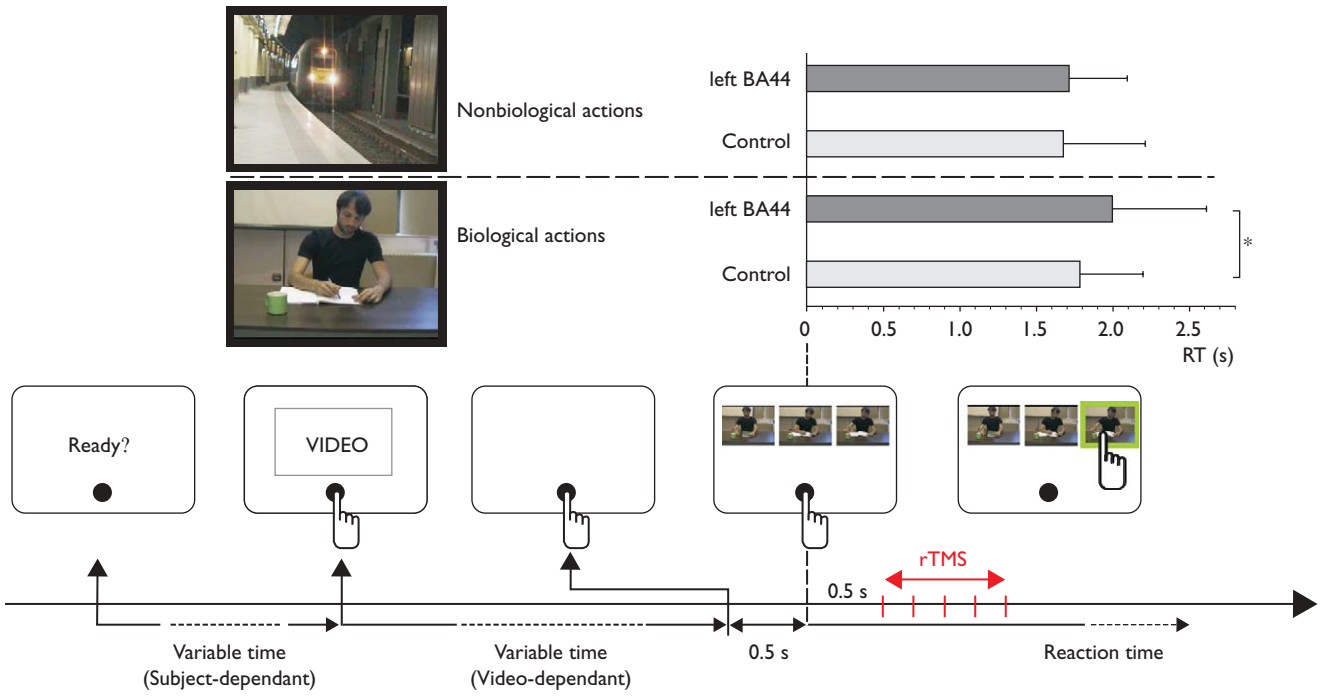
Biological actions	Nonbiological sequences
To open a cupboard by turning the key[a]	A bicycle falling down
To wipe out a blackboard[a]	An automatic drill
To turn one's head and to point	A door closing
To serve a cup of tea[a]	An espresso machine
To open a wallet and take out a piece of paper[a]	A ball rolling down an inclined plane
To get up from the ground[a]	A lamp bubbling
To grab a bottle	A compact disc player
To cut a sheet of paper with a pair of scissors[a]	A moving train
To approach a wall on all fours and touching it	A miniature car rolling
To bow	A bouncing ball on the ground
To take off one's glasses[a]	An escalator
To opening a notebook and write[a]	A Venetian blind
To climb a ladder to get a box[a]	A turning coin
To get over a scaffolding	A burning piece of paper
To touch the tip of one's nose	A wheelchair

[a]Biological stimuli classified as 'transitive and syntactic'.

Transcranial stimulation

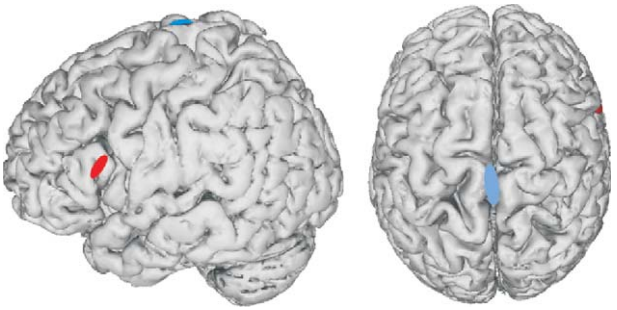
rTMS (110% of resting motor threshold of the first dorsal interosseus muscle, 5 Hz, five pulses) was delivered 500 ms after the display of the three pictures over left BA44 and, as a control site, over the leg representation

Fig. 1



Experimental procedure and effect of left BA44 virtual lesions on reaction times. Bottom: time course of a trial. Each trial started with the display of a message ('Ready?') that instructed the participant to put his/her right index finger on the circle displayed at the bottom of the touch screen, a position he/she had to keep until the display of the three pictures (see below). This contact of the index finger with the touch screen triggered the display of a short video clip (duration: 1–48 s) showing either a biological action or a nonbiological sequence (see Table 1 for the full list). At the end of the video, a blank screen appeared for 500 ms, followed by three pictures extracted from the video clip. The participant had to point toward, and touch, the picture showing the middle of the biological action or of the nonbiological sequence. When the answer was correct, the selected picture was surrounded by a green frame; in case of an incorrect response, the frame was red. The next trial started after a 1-s delay. Repetitive transcranial magnetic stimulation (rTMS) (5 Hz, five pulses, shown in red) was delivered 500 ms after the display of the three pictures either over the left BA44 or over the leg representation of the primary somatosensory cortex (control). Upper right corner: histograms showing the mean reaction times (RT) and standard deviation (SD) in different conditions across participants ($n=13$) for biological and nonbiological sequences. *Significant results ($P<0.05$).

Fig. 2



Mean location of stimulation sites. The two stimulation sites were the pars opercularis of the inferior frontal gyrus (left BA44, red ellipse) and, as a control site, the part of the primary somatosensory cortex located near the midline, corresponding to the representation of the lower limb (S1 leg, blue ellipse). Each ellipse is centered on the mean Montreal Neurological Institute gathered for all participants. The average of coordinates (mean ± SD of *x*, *y*, and *z*) for left BA44 were −59.1 ± 2.6, 16.4 ± 3.8, 20.6 ± 4.7 mm, and −2.7 ± 2.4, −20.5.4 ± 8.5, 74.9 ± 5.9 mm for S1 leg. The surface of the ellipse represents the 95% confidence interval of the normalized coordinates calculated for each participant.

of the primary somatosensory cortex (S1 leg). A neuronavigation technique was used to determine and record the coil position for each participant [14] (see Fig. 2 for averaged locations and coordinates of stimulation sites).

Statistical analysis

The effect of BA44 TMS on error rate and RT was analyzed by means of repeated measures analysis of variance ($ANOVA_{RM}$) with 'site' (left BA44 and S1 leg) and 'type' (biological and nonbiological video) as within-subject factors. Post-hoc comparisons were performed using Tukey's paired *t*-tests. This statistical analysis was performed twice; first, on all trials and second, on a subset of human action trials, as described in Results.

Results

When considering all biological trials together, the $ANOVA_{RM}$ type (2) × site (2) showed a main effect of the type [$F(1,12) = 20.94$, $P < 0.001$] on RT and the post-hoc test indicated that RT in biological trials were significantly longer than in nonbiological trials. However, this analysis failed to show a main effect of site and a significant interaction ($P > 0.1$).

In a second analysis, we categorized the biological actions according to the following criteria: (i) the presence of a hand-object interaction (transitive vs. intransitive actions) and (ii) the presence of a complex structure, that is, an action combining several individual motor acts (syntactic vs. nonsyntactic actions). Only the biological actions that met both criteria (i.e. transitive and syntactic actions, $n = 9/15$, 36 trials/participants) were taken into account in this second analysis and were compared with the nonbiological trials. The $ANOVA_{RM}$ type (2) × site (2) showed a main effect of the type [$F(1,12) = 29.72$, $P < 0.001$], as already reported earlier, but also revealed a significant interaction [$F(1,12) = 6.60$, $P = 0.024$] between type and site. A post-hoc analysis showed that TMS delivered over left BA44 led to longer RTs for syntactic and transitive biological actions, when compared with the control condition (d.f. = 12, $P < 0.001$) (Fig. 1).

Attempts to apply the same analysis to differently categorized biological trials (syntactic only, transitive only, or neither syntactic nor transitive actions) have been unsuccessful in revealing a significant interaction. Analyses also failed to show any main effect or interaction on error rate (all $P > 0.5$).

Discussion

We found that a virtual lesion of left BA44 affected only the reordering task for transitive and syntactic biological actions, that is, actions showing both a hand–object interaction and a complex sequencing of individual motor acts. Nontransitive and nonsyntactic actions and nonbiological sequences remained unaffected by left BA44 virtual lesions.

This study differs from the study of Fazio *et al.* [11] in two points. First, we found that left BA44 virtual lesions had no consequence on response accuracy, but affected only RTs, a finding rather common in the TMS studies [15]. Second, when all biological actions were taken into account, no TMS effect was observed for these trials in comparison with nonbiological trials. A possible explanation is that this study unveils the specific contribution of left BA44 to action recognition, thanks to the higher spatial resolution of TMS than lesion studies. It is therefore sensible to assume that the results of Fazio *et al.* [11] were partly biased by the lesion extending to adjacent cortical areas.

Importantly, we found that the processing of biological 'syntactic' actions was affected solely by left BA44 virtual lesions, suggesting that only the structure of biological actions is processed by Broca's area. This is consistent with the conclusion of a previous study using a point light motion paradigm depicting simplified biological motions [16] and showing that only motion cues of biological actions activated the inferior frontal gyrus. Together with our results, this finding may suggest that Broca's area encodes both the sequence and the final goal of biological actions from available cues. Moreover, in the context of the mirror neuron theory [17] we propose that Broca's area may be critical in deciphering the intermediate steps required to understand the final action goal. Indeed, in monkeys, mirror neurons have been proven to match the agent's observed movements onto the observer's motor repertoire [18]. If one admits that any observed action is automatically mirrored, causing the motor system to 'resonate', one could expect that not only the final goal is processed, as often claimed [19], but also some pragmatic

details. Considering that any human action could be regarded as a combination of individual motor acts in which the order of the elements is of extreme importance to give sense to the global action, Broca's area, in addition to its role in extracting the final goal of actions, may also encode the way this goal is achieved.

The present experiment provides new insight into the implication of Broca's area in action observation by highlighting its role in decoding the hierarchical structure of observed actions. A recent study [20] further illustrates the possible link between BA44 and the syntactic organization of actions. In this study, the authors reported that children with autism, a disorder possibly related to a dysfunction of the inferior frontal gyrus [21], show a deficit in understanding the intentions of others during the observation of multistep-organized actions. In addition, it is noteworthy that ideational apraxia, which can be defined as the disturbance of the conceptual organization of complex, sequential, actions [22], could result from a lesion of the left inferior frontal gyrus [23,24].

Finally, the methodological approach used in this study should allow us to explore the possible role of the right homolog of Broca's area in action observation and recognition. Indeed, on the one hand, brain imaging studies have often shown an activation of this area (concomitantly with Broca's area) in such tasks [4,16], but, on the other hand, the pars opercularis of the right inferior frontal gyrus is known to be involved in distinct cognitive functions such as the motor inhibition control and task switching [25]. In the same way, the present paradigm should also allow us to dissociate between the distinct contribution of BA44 and BA45 (anatomically closed to BA44), in action encoding since it has been suggested that BA45 could process hierarchically higher events than BA44 [5].

Conclusion

This study further strengthens the view that the involvement of Broca's area in language, and particularly in syntax processing, might be rooted in its premotor origin, as shown by the finding that actual or virtual lesions of this area led to deficits in pragmatic encoding of observed actions.

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