

Encoding of human action in Broca's area

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Broca's area has been considered, for over a century, as the brain centre responsible for speech production. Modern neuroimaging and neuropsychological evidence have suggested a wider functional role is played by this area. In addition to the evidence that it is involved in syntactical analysis, mathematical calculation and music processing, it has recently been shown that Broca's area may play some role in language comprehension and, more generally, in understanding actions of other individuals. As shown by functional magnetic resonance imaging, Broca's area is one of the cortical areas activated by hand/mouth action observation and it has been proposed that it may form a crucial node of a human mirror-neuron system. If, on the one hand, neuroimaging studies use a correlational approach which cannot offer a final proof for such claims, available neuropsychological data fail to offer a conclusive demonstration for two main reasons: (i) they use tasks taxing both language and action systems; and (ii) they rarely consider the possibility that Broca's aphasics may also be affected by some form of apraxia. We administered a novel action comprehension test—with almost no linguistic requirements—on selected frontal aphasic patients lacking apraxic symptoms. Patients, as well as matched controls, were shown short movies of human actions or of physical events. Their task consisted of ordering, in a temporal sequence, four pictures taken from each movie and randomly presented on the computer screen. Patient's performance showed a specific dissociation in their ability to re-order pictures of human actions (impaired) with respect to physical events (spared). Our study provides a demonstration that frontal aphasics, not affected by apraxia, are specifically impaired in their capability to correctly encode observed human actions.

Keywords: Broca's area; action recognition; mirror-neuron system; frontal aphasia; motor syntax

Abbreviations: IFG = inferior frontal gyrus; LST = Language sequencing task; MRI = magnetic resonance imaging; RT = reaction time; TT = trial time

Introduction

The seminal work of the French neurologist Paul Broca established that the posterior part of the left inferior frontal gyrus (IFG) was of critical importance for speech production. Broca's famous case,

Leborgne, suffered from left frontal damage extending from the inferior part of the third frontal circumvolution to parts of the insula and the striatum (Broca, 1861; Dronkers *et al.*, 2007). Broca's aphasia was thus described as a syndrome characterized by effortful speech production, impairment in melodic line and

articulation, semantic and phonemic paraphasias, telegraphic sentences with reduced and abnormal grammatical forms (Broca, 1861; Alexander *et al.*, 1990; Caplan *et al.*, 1996).

The first empirical evidence that Broca's area is involved in speech production was provided by Penfield and Roberts (1959). These authors demonstrated that the electrical stimulation of Broca's area in awake neurosurgery patients could evoke a complete arrest of ongoing speech. The hot spot for this effect was located in the *pars opercularis* of the IFG (see also Ojemann *et al.*, 1989). Moreover, Dronkers (1996) showed that a lesion affecting the most posterior part of left IFG (involving insula as well) lead to apraxia of speech (AOS). AOS deficit can be defined as a disorder in the motor programming of the speech musculature to produce the correct sound of words in the proper sequence with the appropriate timing.

Recently, a more complex picture of the role played by Broca's area in the language domain has been given. Several studies demonstrated that Broca's aphasics, in addition to their deficits in production, are also impaired in speech comprehension. Deficits are more evident when patients were tested with verbal material requiring syntactical understanding (Caramazza and Zurif, 1974; Alexander *et al.*, 1990; Caplan *et al.*, 1996). The role of Broca's area in understanding speech has been further supported by the work by Schäffler and collaborators (1993, 1996) showing that the electrical stimulation of Broca's area in non-aphasic neurosurgery patients may elicit comprehension deficits of complex verbal commands.

Language-related studies aside, several recent works have found activation of Broca's area in other cognitive domains (for a review see Fadiga *et al.*, 2006) and, more interestingly as far as the objectives of the present study are concerned, in action viewing, action execution and action imitation (Grafton *et al.*, 1996; Binkofski *et al.*, 1999; Iacoboni *et al.*, 1999; Nishitani and Hari, 2000; Buccino *et al.*, 2001; Grèzes and Decety 2001; Baumgaertner *et al.*, 2007). These data have been considered as an empirical support to the existence of a mirror-like system in humans, mapping execution and observation of actions onto the same neural substrate (Rizzolatti and Craighero, 2004). However, some concerns have been raised regarding the conclusions that can be drawn from such techniques and experimental designs (Dinstein *et al.*, 2007; Turella *et al.*, 2008). In fact, the use of a correlational approach cannot provide a final proof of the involvement of Broca's area in the human mirror-neuron system.

A possible answer to the question whether Broca's area could be involved in action understanding might be provided both by neuropsychological studies of brain lesioned patients and by temporary inactivation of Broca's area by transcranial magnetic stimulation (TMS) during action-understanding tasks. Pobric and colleagues (2006) administered TMS on the IFG while subjects had to judge the weight of an object lifted by an actor. Their data show a reduced accuracy in performing the task, in accordance with the hypothesis that the IFG plays an important role in encoding the details of action kinematics. Moreover, several studies on frontal aphasic patients have shown a correlation between lesion location and action-related non-verbal impairments such as recognizing signs, gestures and pantomimes (Duffy and Duffy, 1975; Gainotti and Lemmo, 1976; Daniloff *et al.*, 1982; Varney, 1982;

Glosser *et al.*, 1986; Wang and Goodglass, 1992; Bell, 1994). More recently, Tranel *et al.* (2003), showed that left frontal brain-damaged patients have difficulty in understanding action details when presented with cards depicting various actions, and Saygin *et al.* (2004) have demonstrated a significant correlation between linguistic deficits and the comprehension of actions in patients with different types of aphasia.

It should be noted, however, that although strongly suggestive of a strict relationship between language- and action-related domains, the results by Tranel (2003) and Saygin (2004) were achieved through tasks including some linguistic components (i.e. verbal instructions). Therefore, the reported deficits in the action domain might have, at least partially, been altered by uncontrolled linguistic processes. Furthermore, left fronto-parietal lesions are often associated with praxic disturbances (Goldenberg, 1996). Both studies, unfortunately, did not control for such possibilities, which could act as a critical confounding factor in the light of the recent study by Pazzaglia *et al.* (2008), showing that limb apraxic deficits are often associated to the impairment of gesture comprehension.

As a consequence, on the basis of the current empirical knowledge, a conclusive picture of the causal relationship between Broca's aphasia and action understanding deficits cannot be drawn without doubts. In the present work, we selected frontal aphasic patients (without apraxia) on the basis of lesion localization. We then administered a newly designed task to measure patient's performance in action comprehension without taxing the language system. Patients were requested to correctly sequence some randomly mixed pictures taken from video clips representing human actions or physical events. Our prediction was that Broca's aphasics would exhibit a dissociation in dealing with these two classes of stimuli, thus providing the evidence that Broca's area, beside its linguistic function, is also involved in encoding human actions.

Methods

Participants

Medical records of twenty patients from the community of Ferrara (Department of Neuroscience, University and Hospital of Ferrara, Unit of Neuropsychological Rehabilitation, Italy) were evaluated after obtaining informed consent. Patients were selected if, at the time of the enrolment into the hospital rehabilitation program, they presented a vascular lesion in the territory of the left middle cerebral artery, according to computerized tomography (CT) or magnetic resonance imaging (MRI) data. All of them presented disorders of language production with agrammatic speech (speech was laboured, choppy and poorly articulated), but their comprehension of normal conversation was well preserved. In addition to the testing for aphasia (Ciurli *et al.*, 1996; Capasso and Miceli, 2001; Token test: De Renzi and Vignolo, 1962), patients were screened for the presence of apraxia (De Renzi *et al.*, 1966; De Renzi *et al.*, 1980). Further exclusion criteria included diagnosis or suspicion of dementia, head traumas, brain tumours, multiple infarcts or other neurological conditions. All patients had normal intelligence and had no difficulty in attending to, perceiving or retrieving visual stimuli. According to the evaluation

Table 1 Socio-demographic data and lesion location

Initials	Gender	Age	Education	Main lesions
DF	M	53	8	Frontal (+IFG), temporal, parietal, insula + external capsule region.
FG	M	51	17	Frontal (+IFG), temporal, insula + external capsule region and basal ganglia.
SC	F	27	18	Frontal (+IFG), temporal, insula + external capsule region.
EC	M	56	8	Frontal (+IFG), temporal, insula.
CC	M	61	13	Frontal (+IFG), temporal, insula + external capsule region.
GF	M	60	8	Frontal (+IFG), parietal, insula.

Age, gender and lesion locations of patients that fulfilled the experimental requirements.

of their case history, 11 patients out of the initial 20 were considered for further testing.

The further neuropsychological testing (see below) was aimed at selecting patients with a high degree of cognitive functionality and with normal praxic capabilities. Following this second-level, more restrictive testing, the number of patients recruited for the final experimental phase was reduced from eleven to six. The age of recruited patients ranged from 27 to 61 (mean 51 ± 12.5 SD) and their average level of education was 12 ± 4.7 years. Socio-demographic data and lesion location, as assessed by the local neuroradiology unit, are provided in Table 1. At the time of our investigation, these patients presented a stable lesion due to cerebro-vascular accident, which had occurred 3–6 years before the enrolment, and none of them had been included in other studies. As a control group we selected six adult participants matched for age, handedness and education level, with no history of neurological or psychiatric disorders. All of them had normal or corrected-to-normal vision and hearing. The control group had a mean age of 50.2 ± 13.1 and a mean educational level of 12.7 ± 4 years. The procedures used in the study were in agreement with the guidelines of the University of Ferrara Ethical Committee and with the Declaration of Helsinki.

Neuropsychological testing

Patients were tested by a skilled neurologist in a quiet room reserved for experimental purposes, in the neuropsychological rehabilitation unit. We collected a series of reduced versions of standard neuropsychological questionnaires aimed at specifically and rapidly testing a wider range of cognitive functions. This test was administered both to the eleven patients and to the control subjects. The main goal of this procedure was to select patients with a high degree of cognitive functionality. The test included three main sections—one testing general abilities, the second concerning praxis and the third related to the language domain. The first section included items evaluating calculus, memory span and rhythm generation as well as the general sense of direction (questions such as: 'Where are we now?', 'Why we are here?', 'What day of the week is today?'). The praxic section had 29 items with a cut-off level of 18 correct responses. The testing included: (i) imitation of distal intransitive movements; (ii) imitation of intransitive movements of the mouth area; (iii) imitation of transitive movements; (iv) execution of intransitive sequence of movements upon verbal instruction; and (v) pantomime. The language section included 67 items with a cut-off level of 18 correct responses. The complete set included: (i) denomination of visually presented natural and manufactured objects and tools; (ii) repetition of words and pseudo-words following audio-visual and auditory presentation; (iii) verbal fluency; and (iv) auditory comprehension testing. This collection of tests was administered prior to the experimental session and only six patients met the second enrolment criteria for

participating in the study. The whole experimental session was videotaped for further offline analysis. We then visually inspected each movie in order to exclude the presence of any sub-clinical apraxic signs. Particular attention was devoted to the exclusion of deficits regarding the temporal and spatial sequencing of an action or the loss of object knowledge. This offline analysis was carried out by two independent professional neuropsychologists. The outcome of this additional evaluation confirmed previous examinations.

Lesion analysis

To anatomically characterize the brain lesion, all recruited patients underwent an additional specific MRI session at the beginning of the study. MRI images were acquired through three-dimensional-fast spoiled gradient recalled (3D-FSPGR) T_1 -weighted sequence (TR 12.6 ms, TE 2.7 ms, TI 400 ms, FOV 250 mm \times 250 mm, thickness 0.6 mm, gap: 0.6 mm, 256 \times 256 matrix, 250 slices). The graphical outline of the lesions and the co-registration of individual brains in standard stereotaxic space were performed offline using MRICro software (Rorden and Brett, 2000). We transformed each anatomical image into a standard stereotaxic space using the co-registration method (non-linear warping) provided by SPM 96. Brain lesions were mapped in the MNI stereotaxic space using the standard MRI volume redefined by Colin's Atlas (Evans *et al.*, 1993). After individual co-registration, the lesioned areas of each patient were superimposed onto each other by means of the specific tool provided by MRICro software. We thus obtained the region of superimposition common to all the patients shown in red in Fig. 1A. The higher lesion overlap of this region was centred in the *pars opercularis* of the IFG (BA44), as shown by the probabilistic atlas of BA44 by Amunts *et al.* (1999) (Fig. 1B and C).

Experimental design, materials and procedure

Participants sat comfortably in front of a touch screen monitor (MicroTouch M170, 3M Touch Systems, Inc.). They were informed of the experimental procedure and completed a first practice trial under the experimenter's guidance. The experimental interface was run on a PC using custom made software. All experimental events and their relative timing were automatically recorded during each trial and stored on the hard-disk for further offline analysis. Each trial began with a message displayed on the computer screen inviting the participant to press a key to start the trial. A videoclip was then displayed on the screen and the participant was instructed to pay attention to it. At the end of the videoclip, after a delay of 0.5 s with black screen, four images taken from the same video were presented simultaneously at four different spatial locations

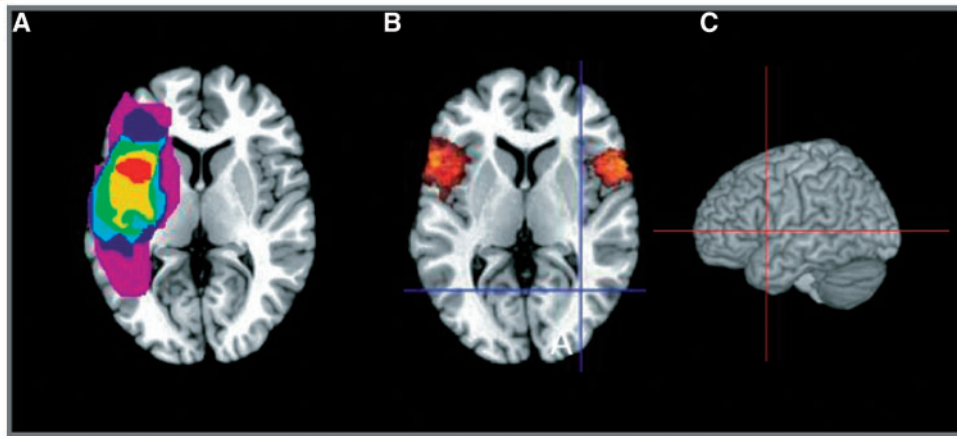


Figure 1 Anatomical location of patient's lesions. (A) shows the overlays of the six patients' lesions on the Colin's template brain, where different colours represent each patient, (B) shows the probabilistic extension of Broca's area as identified by Amunts *et al.* (1999), on the same horizontal slice and (C) shows the 3D rendering of the Colin's standard brain with the overlap of lesions marked with a red cross on the surface. Note that the overlap corresponds perfectly with the *pars opercularis* of the IFG (BA44).

(upper left, upper right, lower left and lower right). At this point subjects were asked to organize the four snapshots in a meaningful temporal order, by touching the screen. As soon as two snapshots were touched sequentially, their spatial location on the screen was swapped. When participants considered they had accomplished the trial, they had to press a validation button. All subjects were instructed to be as accurate as possible and, only in the second instance, to complete the task as fast as possible. The particular stress given to accuracy was justified by the observation that some patients had more difficulty when temporally pressed, also depending on the severity of their clinical picture.

Participants were requested to constantly focus their attention on the task and, after each trial, were asked whether they needed a rest. Generic motivational feedback (e.g. 'you are doing great so far', 'very good') was given as often as considered necessary to keep participants engaged in the task (approximately once every trial). Feedback regarding the accuracy of the performance ('OK!' or 'Fail!') was given on the computer screen at the end of each trial. At the end of each trial, subjects were also asked to explain what the video clip was about, to verify that they could understand the global meaning of the stimuli.

The following variables were recorded: accuracy (degree of correct sequencing), reaction time (RT) and trial time (TT). Accuracy measured whether the order of the snapshots, generated by the subjects, was correct or not (in percentage). RT was the amount of time elapsed from presentation of the snapshots to the first touch of the screen. TT was the amount of time between presentation of the snapshots and pressing of the validation button.

Sequencing task

The same task was administered to both patients and controls. The video clips were subdivided into two different classes: human actions and physical events. Human actions stimuli were transitive and intransitive actions performed by a human agent (e.g. hand-grasping of a bottle, head-turning and pointing, etc.). Video clips of physical events represented common life dynamic events, such as a bicycle falling on the floor or a door opening by itself. Snapshots were selected for each video clip by the experimenters, paying attention to provide enough cues for the successive sequencing task (see Fig. 2 for a pictorial description of the task).

Nineteen videos (Table 2), plus one used to familiarize the participants to the experimental procedure, were used during the experiment. In order not to overload the patient's attention, we restricted the number of videos by unbalancing the number of stimuli of the two categories (human actions: 14 and physical events: 5). This decision was taken after a pilot experiment on 13 healthy subjects using a larger set of 30 movies. We found that physical events, on average, led to a smaller variability of the time necessary to accomplish the task (i) and of the time to begin sequencing the four pictures (ii) [standard deviation (SD) (i) 4.52 s; (ii) 4.02 s for human actions and (i) 2.29 s; (ii) 1.68 s for physical events]. However, task difficulty could be better described by absolute time values, rather than SD. In fact, SD indicates how variable performance is across different subjects, whereas mean values describe how difficult the task was in all subjects. Therefore, we reduced the number of items in the least variable condition (physical events) but selected those trials that, according to mean values, were homogeneously spread across the difficulty continuum (Table 2).

Language sequencing task

Patients also underwent a second testing phase. Their task was similar to that outlined previously, but the stimuli differed. The videoclips were replaced with either written sentences (8) or single words (20). Their task was to sequence four scrambled written segments taken from the stimuli. Sentences were divided into simpler constituents (i.e. Press/the button/to open/the door) and words into syllables (i.e. Cam/mi/na/re: to walk).

Statistical analysis

A Mann–Whitney U-test was used to analyse the neuropsychological data obtained from both patients and normal controls for each sub test. The null hypothesis was that the two samples are drawn from a single population, and therefore their performance is similar. Three two-way repeated-measure ANOVAs were performed on RT, TT and Accuracy, with a between-subjects factor GROUP (Aphasics, Controls) and a within-subject factor CONDITION (human actions, physical events). Fisher's LSD *post hoc* comparisons were then conducted when factors showed a significant effect. Furthermore, a linear correlation analysis was run between patient performance in the

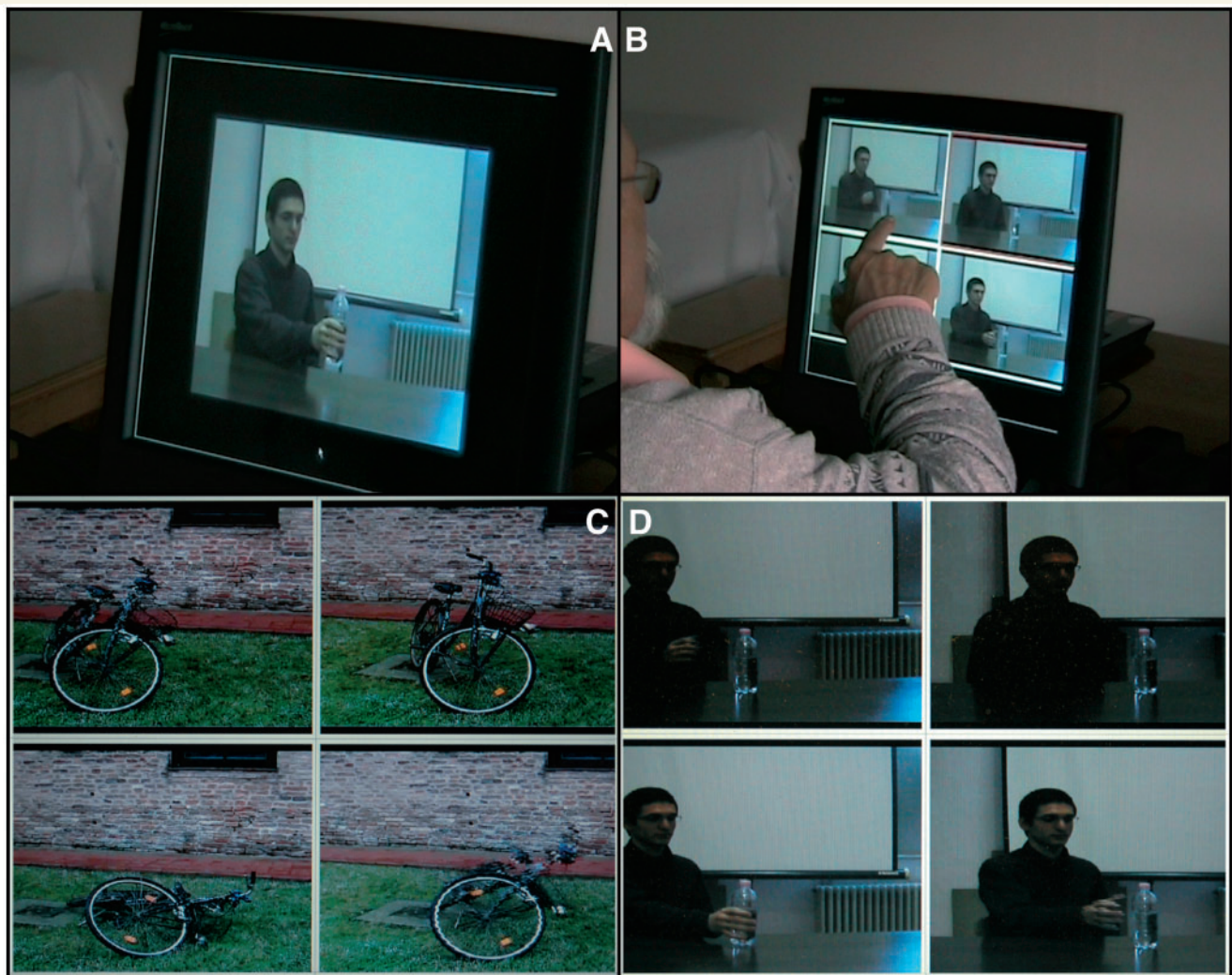


Figure 2 Experimental set-up and task. (A) The videoclip is presented on the screen, (B) Four snapshots are presented at the four corners of the screen, (C) Example of physical events snapshots and (D) Example of Human Actions snapshots.

sequencing task and in the language sequencing task (LST). This analysis served to measure whether there was a performance correlation across the two tests. All the analyses were performed using Statistica 6 (StatSoft, Inc.).

Results

The score in the neuropsychological test battery was on average 23.5 out of 29 items on the apraxia section with a SD of 2.88. The controls obtained 28.5/29 and a SD of 0.55. The language section showed a performance of 43.5 out of 67 with a SD of 15.1 for patients, while controls scored on average 64.67 out of 67 items and a SD of 1.63. Among all neuropsychological tests, the denomination of tools, actions and tool use showed a significantly worse performance in patients ($U=32.5$, $P<0.05$, $U=36$, $P<0.01$ and $U=25.5$, $P=0.24$, respectively), whereas denomination of natural objects was not impaired ($U=25.5$, $P=0.24$).

Table 3 shows the performance of patients and controls on these items of the neuropsychological questionnaire.

The ANOVA on RTs [main effect: CONDITION, $F(1,5)=1.675$; $P=0.25$. GROUP: $F(1,5)=15.95$; $P=0.01$; Interaction CONDITION \times GROUP, $F(1,5)=0.026$; $P=0.88$] as well as the ANOVA on TT [main effect: CONDITION, $F(1,5)=0.406$; $P=0.55$. GROUP: $F(1,5)=24.665$; $P=0.004$; Interaction CONDITION \times GROUP, $F(1,5)=0.439$; $P=0.54$] showed a significant effect for factor GROUP, indicating that patients were generally slower than controls, independent of the experimental manipulation (physical events or human actions). The speed of performance (RT and TT) was not specifically influenced by the experimental condition (human actions and physical events), except for the fact that the healthy controls were consistently faster than the patients. This speed bias can easily be accounted for by the general increase in reaction times and in movement times often observed in brain-lesioned patients (Benton, 1986).

More interestingly, ANOVA performed on Accuracy showed a significant effect for the interaction GROUP \times CONDITION

Table 2 Stimuli list

Stimuli	RT	TM	TT
Touching the tip of one's nose	2.133 ± 0.724	7.058 ± 5.125	9.191 ± 5.017
A bow	2.317 ± 1.354	4.683 ± 2.46	7 ± 2.9
Climbing a ladder to get a box	2.358 ± 0.643	7.767 ± 3.515	10.125 ± 3.908
A bicycle falling*	2.459 ± 0.525	4.017 ± 0.653	6.475 ± 0.918
Approaching a wall on all fours and touching it	2.484 ± 0.759	5.725 ± 1.75	8.208 ± 1.436
Plotter*	2.691 ± 1.21	4.267 ± 2.331	6.958 ± 2.536
Grabbing a bottle	2.767 ± 1.226	7.208 ± 3.008	9.975 ± 4.065
Turning one's head and pointing	2.991 ± 1.431	5.467 ± 3.307	8.458 ± 3.413
Cutting a sheet of paper with a pair of scissors	3.208 ± 1.291	6.075 ± 1.872	9.283 ± 2.081
Opening a wardrobe by turning the key	3.392 ± 1.572	10.392 ± 7.347	13.783 ± 6.739
Opening a notebook and writing	3.508 ± 1.185	10.975 ± 6.818	14.483 ± 7.274
A remote controlled car against a wall*	3.667 ± 1.593	6.542 ± 1.52	10.208 ± 1.723
Getting over an obstacle	3.725 ± 1.346	6.258 ± 3.058	9.983 ± 3.128
Getting up from the ground	3.783 ± 2.137	7 ± 2.607	10.783 ± 4.322
A door closing*	3.95 ± 2.457	5.692 ± 1.69	9.642 ± 3.458
Taking off one's glasses	3.975 ± 1.47	7.45 ± 5.832	11.425 ± 6.943
A ball rolling down an inclined plane*	4.1 ± 1.762	6.517 ± 2.203	10.617 ± 2.823
Wiping out a blackboard	4.133 ± 1.967	8.7 ± 5.328	12.833 ± 6.041
Opening a wallet and take out an ID	4.158 ± 2.233	5.933 ± 2.753	10.092 ± 4.455

List of 19 movies presented to both patients and matched controls. RT, TM, TT and relative SD for each stimulus, measured during the pilot experiment in 13 subjects, are provided. Asterisks denote physical events stimuli.

Table 3 Neuropsychological testing performance for action-related items

Denomination	Objects	Tools	Tool uses	Action
Patients				
FG	3	1	0	0
GF	11	5	3	3
SC	12	7	4	6
CC	9	1	2	0
DF	10	4	0	2
EC	12	5	6	6
Mean	9.5/12	3.83/8	2.5/8	2.83/8
Control				
AF	12	8	8	8
GB	12	7	8	8
VG	11	6	8	8
VV	12	8	8	8
ES	11	6	8	8
MT	11	6	8	8
Mean	11.5/12	6.83/8	8/8	8/8

Patient's and matched control's performance on denomination of objects, actions, tools and tools use items present in the neuropsychological testing. Performance between the two groups did differ significantly in all items but not in the denomination of natural objects.

[$F(1,5)=12.594$; $P=0.02$], but no significant effect for factor GROUP [$F(1,5)=4.314$; $P=0.09$] and CONDITION [$F(1,5)=0.0005$; $P=0.98$]. *Post hoc* comparisons showed that while the control group performed equally well in the two experimental conditions (correct response for human actions: 0.89 ± 0.04 ; correct response for physical events 0.77 ± 0.06 SEM; $P=NS$), aphasics' performance showed a trend to significance ($P=0.05$) between human actions (0.64 ± 0.11) compared with physical

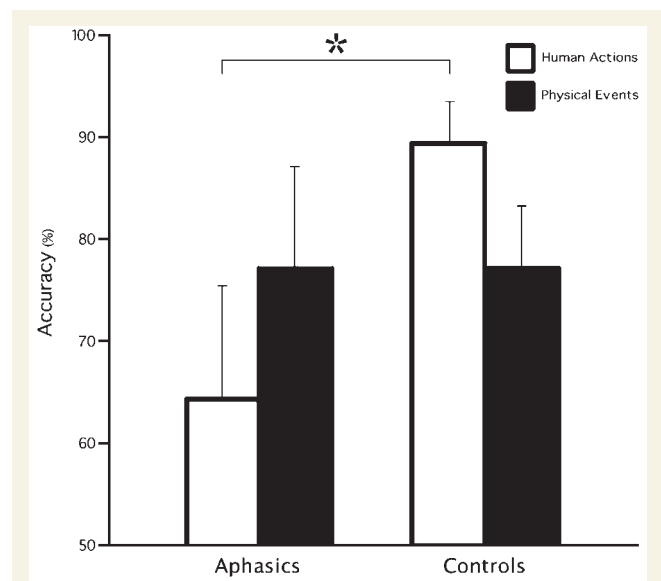


Figure 3 Accuracy results. Histograms depict the accuracy ratio in aphasic patients (Aphasics) and normal subjects (Controls) for both human actions (white bars) and physical events (black bars) conditions. Whiskers indicate the standard error of the mean. Asterisks denote statistically significant differences ($P < 0.05$) in accuracy ratio between aphasics and controls in the human action condition.

events (0.77 ± 0.10), and a highly significant difference with respect to controls for the human action condition ($P=0.004$) (Fig. 3).

A further analysis was carried out on the intransitive versus transitive human action trials. To this purpose, we separated

patients' and controls' data into transitive ($n=8$) and intransitive trials ($n=6$). As transitive video clips we defined hand-object interactions (e.g. grasping a glass). The intransitive video clips were those representing meaningful actions but without object (e.g. turning the head and point). Paired t -tests showed that patients were significantly impaired with respect to controls in both transitive ($P=0.04$) and intransitive trials ($P=0.001$), without any difference in performance between transitive and intransitive trials ($P=0.37$). Therefore, results cannot be due to the presence of a human-object interaction, since a similar impairment was also present for the intransitive human actions.

The language sequencing test showed a severe impairment for patients in the verbal domain and low accuracy levels in reorganizing scrambled sentences or syllables (LST, mean percentage of correct responses \pm SEM: All LST: 53.15 ± 12.24 ; sentences: 52.08 ± 15.95 ; syllables: 53.64 ± 12.41), confirming their deficits in the language domain. Moreover the correlation analysis between the action- and language-sequencing test showed a significant relation between performance in sequencing transitive, human action video clips and all items of the language sequencing test ($r^2=0.74$; two-tailed $P=0.03$). Conversely, performance in the sequencing of intransitive actions and physical events was not correlated with the language sequencing test (Intransitive actions: $r^2=0.04$; two-tailed $P=NS$; physical events: $r^2=0.15$; two-tailed $P=NS$).

Discussion

The present work shows that frontal aphasic patients, characterized by a lesion centred in the left *pars opercularis* of Broca's region and by the absence of apraxic symptoms, are specifically impaired in sequencing pictures representing actions (transitive or intransitive) performed by a human agent but not in sequencing physical events. Additionally, their reduced ability to sequence sentence segments and word syllables correlated with the impairment in sequencing transitive actions. Although, it is still possible that plastic processes and/or compensatory strategies might take advantage from the right homologue region, patients did not restore these specific abilities.

Why are these patients not able to solve the sequencing task for human actions only? In our experiment, subjects were requested to understand what they were observing in the video clip, and then order single snapshots into a meaningful sequence. To do this, we suppose the subjects had to represent (and replay) the rules connecting critical information presented in the videos. The interpretation we favour is that, to correctly sequence human actions, subjects were implicitly mapping the observed actions onto their own motor repertoire. In other words, the subjects had to gain access to 'how' a given action was composed in terms of simple units, and harmonically (and pragmatically) restructure it through an embodiment process. Conversely, in the case of physical events, such an implicit and embodied motor representation was unnecessary to solve the task. This interpretation is in line with the finding that similar results were achieved in sequencing both transitive and intransitive actions, and complement the idea that the human-object interaction is not a necessary prerequisite

to activate the motor system during action observation (Fadiga *et al.*, 1995). More interestingly, patients' performance in human action sequencing was also correlated to their deficit in sequencing words forming sentences and syllables forming words. Moreover, they all had severe problems in naming tools and, more importantly, tools' uses. On the contrary, patients' understanding of the global meaning of the observed actions was mostly preserved if they were asked to explain what they had seen.

Why should this capacity of representing action pragmatics be encoded in Broca's area? A large number of recent neuroimaging and neurophysiological studies have shown that a reproducible network of cortical areas, comprising Broca's region, becomes active during action observation (for a review see Rizzolatti and Craighero, 2004; for a critical position on the possibility to consider these activations as a proof of the existence of a human mirror-neuron system see Turella *et al.*, 2008).

This productive area of research has been motivated by previous monkey studies describing similar mechanisms at a cellular level in macaque premotor area F5 (di Pellegrino *et al.*, 1992; Gallese *et al.*, 1996; Rizzolatti *et al.* 1996) and in the inferior parietal lobule (Fogassi *et al.*, 2005; Rozzi *et al.*, 2008).

Frontal and parietal mirror neurons found in the macaque brain fire when the monkey executes an action and also when it observes the same action performed by someone else. It has been suggested that mirror neurons may provide the brain with an implicit knowledge about the meaning of actions because seen actions are directly matched onto the observer's motor repertoire. Therefore, the finding that Broca's area, the putative human cytoarchitectonic homologue to monkey area F5 (Petrides and Pandya, 1997; Petrides *et al.*, 2005), becomes active during action observation, strongly supports the hypothesis that it may form a crucial node of the human mirror-neuron system. It could be a wrong, or at least too simplistic a conclusion, to think that Broca's area and its monkey homologue share all their functional properties. Indeed, evolution is characterized by an increase of cytoarchitecturally diverse cortical areas. For this reason, the functional properties of monkey area F5 might have been distributed to different sectors of the human premotor cortex, probably according to their degree of response complexity. However, functional and anatomical evidence reinforce the intriguing possibility that the goal-related action vocabulary stored in monkey premotor cortex (Rizzolatti *et al.*, 1988) and the syntax-related properties of Broca's area, might be evolutionarily linked. In our view the data presented by our work strengthens this link by providing, for the first time, clear evidence that Broca's aphasics show a significant impairment in representing observed actions.

Actions, by definition, are hierarchical compositions of simpler motor acts (Grafton and Hamilton, 2007) aiming at a goal. Thus, action decoding via visual information may require the harmonic composition of low level visual-kinematic features into a high level representation of action-goals and therefore of agent's intention. The same intention can be conveyed by a set of movements with quite a large degree of inter- and intra-subject variability, which the system has to efficiently categorize as pertaining to the same action. What remains constant and so critically useful, are the rules

to compose such hierarchically lower units. We might consider this set of rules as a sort of motor syntax, the knowledge of which is, in our view, necessary to solve our sequencing task in the case of human actions but not in that of physical events.

In agreement with our interpretation, Dominey *et al.* (2003) and Sirigu *et al.* (1998) demonstrated that patients with lesions of Broca's area are impaired in learning the hierarchical/syntactic structure of linguistic sequential tasks. Moreover, and more recently, an event-related fMRI study succeeded in disentangling hierarchical processes from temporally nested elements (Koechlin and Jubault, 2006). These authors reported that Broca's area, and its right homologue, control selection and nesting of action segments, integrated in hierarchical behavioural plans, regardless of their temporal structure. Finally, Bahlmann *et al.* (2008) showed that, when comparing the processing of hierarchical dependencies to adjacent dependencies in an artificial language, significantly higher activations were observed in Broca's area and in the ventral premotor cortex. These results indicate that Broca's area may form a node of a neural circuit responsible for processing hierarchical structures in an artificial grammar context.

In our view, Broca's area might have specialized in encoding complex hierarchical structures of goal-directed actions, and to eventually apply these pragmatic rules to more abstract domains. Therefore, the language-related functions sub-served by Broca's region could be the most eloquent part of a more general computational mechanism shared by multiple domains. Such mechanisms could be imagined as a polymodal syntax (Baumgaertner *et al.*, 2007) endowed with the ability to organize and comprehend hierarchically dependent elements into meaningful verbal and non-verbal structures.

Conclusions

The present work sheds light on the functional role of Broca's area by providing evidence that, in the absence of apraxia, a lesion affecting Broca's area impairs the ability to sequence actions in a task with no explicit linguistic requirements. Here, we propose that the complex pattern of abilities associated with Broca's area might have evolved from its premotor function of assembling individual motor acts into goal-directed actions. This capacity of dealing with complex motor hierarchical structures could have evolved into a polymodal syntax serving also higher cognitive functions sharing with action some basic grammatical rules. Consequently, we speculate that an ancient motor syntax might have evolved into a 'supramodal syntax', at the basis of the 'modern' linguistic one.

Funding

European Community grants (CONTACT-NEST Project 5010, ROBOTCUB-IST-004370, POETICON-ICT-215843); Italian Ministry of Education grants (to L.F.).

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