Neural basis of pantomiming the use of visually presented objects

Raffaella I. Rumiati,[a,b,*] Peter H. Weiss,[b,c] Tim Shallice,[a,d] Giovanni Ottoboni,[a] Johannes Noth,[c] Karl Zilles,[b,e] and Gereon R. Fink[b,c]

[a] *Cognitive Neuroscience Sector, Scuola Internazionale Superiore di Studi Avanzati (S.I.S.S.A.), via Beirut 2-4, 34014 Trieste, Italy*
[b] *Institute of Medicine, Research Center Jülich, D-52425 Jülich, Germany*
[c] *Department of Neurology, University Hospital, RWTH, D-52074 Aachen, Germany*
[d] *Institute of Cognitive Neuroscience, 17 Queen Square, University College, London, WC1 3AR, UK*
[e] *C. and O. Vogt Institute for Brain Research, University of Düsseldorf, D-40001 Düsseldorf, Germany*

Neuropsychological studies of patients suffering from apraxia strongly imply a left hemisphere basis for skilful object use, the neural mechanisms of which, however, remain to be elucidated. We therefore carried out a PET study in 14 healthy human volunteers with the aim to isolate the neural mechanisms underlying the sensorimotor transformation of object-triggers into skilled actions. We employed a factorial design with two factors (RESPONSE: naming, pantomiming; and TRIGGER: actions, objects) and four conditions (IA: imitating the observed pantomime; IO: pantomiming the use of the object shown; NA: naming the observed pantomime; NO: naming the object shown). The design thus mainly aims at investigating the interaction [i.e. (IO−IA)−(NO−NA)] which allows the assessment of increased neural activity specific to the sensorimotor transformation of object-triggers into skilled actions. The results ($P < 0.05$, corrected) showed that producing a wide range of skilled actions triggered by objects (controlled for perceptual, motor, semantic, and lexical effects) activated left inferior parietal cortex. The data provide an explanation for why patients with lesions including left parietal cortex suffer from ideational apraxia as assessed by impaired object use and pontomining to visually presented objects (Brain 111 (1988) 1173; Cogn. Neuropsychol. 18 (2001) 671).

Introduction

One of the most basic of all human cognitive skills is the ability to use a very large range of objects by making sequences of object-specific actions: Although skilful object use has been observed in chimpanzees, apes are highly restricted in the variety of their habitual tool use (McGrew, 1993). Neuropsychological studies of patients suffering from apraxia suggest that this human capacity for

highly skilful object use is a left hemisphere function (De Renzi et al., 1968; Liepmann, 1905). A range of different conceptual frameworks has been used since to further characterize apraxia. One group of authors has adhered to Liepmann's original suggestion that one should distinguish between ideomotor and ideational apraxia. Patients with ideational apraxia suffer from a deficit of performing object-related skilled actions (De Renzi and Lucchelli, 1988; De Renzi et al., 1968; Lehmkuhl and Poeck, 1981).

Acquiring skills in object use involves a variety of aspects. In many cases such as driving a car, it requires the development of a complex hierarchy of control structures, (which incidentally may also be present in apes, see Byrne, 2002). In others, such as those involved in many sports, exquisite timing in response to external triggers must be attained (see, e.g., McLeod, 1987). In yet others such as those needed in carpentry, it requires knowledge of naïve physics (Goldenberg and Hagmann, 1998). One key ability common to all these skilful actions is, however, to acquire a set of routines each corresponding to specific learned components of a skill. In a more theoretical language, these routines could correspond to specific sets of parameter settings within a general system for the control of action, such as that suggested by Wolpert and Ghahramani (2000). A second key ability is to be able to elicit each of these components by a specific perceptual trigger (or triggers). When, for instance, a patient is presented with an object, and asked to use it (or to pantomime its use), he or she must have learned both the appropriate movement and its eliciting condition. For the second of these key abilities, it is well established that even low-level (visual) object characteristics may help to elicit an action appropriate to an object—Gibson's (1979) concept of affordance. In humans, the existence of such object-triggered affordances is supported by both experimental (Rumiati and Humphreys, 1998; Tucker and Ellis, 1998) and neuropsychological (Humphreys and Riddoch, 2002; Riddoch and Humphreys, 1998) evidence. Object-specific triggering cannot, however, just depend upon the low-level visual characteristics of objects; just consider the actions elicited by an electric plug, an electric iron, and so on.

The conceptual framework of Norman and Shallice (1980) extends the affordance concept by postulating the existence of an object trigger system which activates specific action schemata. A basic biased competition mechanism—called contention schedul-

* Corresponding author. Cognitive Neuroscience Sector, Scuola Internazionale Superiore di Studi Avanzati (S.I.S.S.A.), via Beirut 2-4, 34014, Trieste, Italy. Fax: +39-040-3787615.
E-mail address: rumiati@sissa.it (R.I. Rumiati).
Available online on ScienceDirect (www.sciencedirect.com.)

ing and implemented in Cooper and Shallice (2000)—then allows routine actions to be produced without conflict by activating relevant and inhibiting irrelevant schemata at appropriate times set by environmental triggers. Thus, a neuropsychological deficit observed in patients with left hemisphere lesions who show ideational apraxia (defined as a selective deficit in performing highly practiced actions involving objects; De Renzi and Lucchelli, 1988; Liepmann 1905; Rumiati et al., 2001) can be interpreted as damage to or a disconnection between components of this system.

The complexity of the set of processes involved in the production of skilled actions is very difficult to analyze by standard lesion methods as complex skilful actions depend upon and modulate the already complex set of processes required in more basic visuomotor operations. In addition, neuropsychological attempts to analyze the neural basis of skilful object use have proved difficult because patients tend to have rather large lesions and additional deficits, for example, impaired imitation of actions, action or object agnosia, or aphasia. This neuropsychological dilemma (see Marshall and Fink, 2003) provides a special opportunity to use functional imaging to elucidate the organization of these subsystems which when damaged give rise to the relevant neuropsychological disorders. So far, however, functional imaging of object use has been limited to a highly restricted set of very simple actions such as grasping (Grafton et al., 1996a), also using various forms of grip (Grèzes et al., 2003), the manipulation of meaningless objects (Binkofski et al., 1999; Grefkes et al., 2002), learning of one specific set of movements (Jenkins et al., 1994; Stephan et al., 1995), or has used the analogy of "mental simulation" of the actions (Decety et al., 1994; Grafton et al., 1996b; Stephan et al., 1995).

In this paper, we primarily aim at investigating whether there is evidence for specific mechanisms underlying the triggering of actions by objects. This is strongly suggested by neuropsychological evidence of utilization behavior following medial prefrontal lesions (Lhermitte, 1983; Shallice et al., 1989). However, the locus of lesions which give rise to such effects—medial prefrontal cortex (see De Renzi and Barbieri, 1992)—corresponds to the impairment of parts of a Supervisory System which inhibits any such behavior rather than of the trigger system itself. It is therefore not relevant for localizing the trigger system. Based on animal neurophysiological data (Rizzolatti et al., 1997; Sakata et al., 1995; Taira et al., 1990), functional imaging studies (Binkofski et al., 1999; Grafton et al., 1996a; Grefkes et al., 2002) and, to some extent, neuropsychological studies of patients suffering from ideational apraxia (De Renzi and Lucchelli, 1988; Rumiati et al., 2001), a more plausible hypothesis for the locus of the trigger system for action schemata, could be left inferior parietal cortex.

A major technical problem when employing functional magnetic resonance imaging to study the neural mechanisms underlying skilled actions is the production of movement artifacts as a result of performing the task. This has led some investigators to use tasks in which subjects are required to imagine performing the action (Decety et al., 1994; Grafton et al., 1996b). In contrast, PET is less sensitive to movement artifacts and thus allows the assessment of proper skilful actions in the scanner. We accordingly performed a study in which normal volunteers produced 90 different skilful object-related pantomimes while lying in a PET scanner. We used pantomiming of object and tool use (rather than actual object and tool use) as this task predicts well and correlates with performance on actual object and tool use in apraxia (De Renzi and Lucchelli, 1988; Goldenberg and Hagmann, 1998), but avoids practical problems such as object placement in the subjects'

hands which causes difficulties in the scanning environment (e.g. timing, the necessity to have another person in the scanning room, etc.). In addition, it has been established in neuroimaging studies that the mere viewing of objects affords actions that can be performed with them (Grèzes and Decety, 2002). To isolate the neural mechanisms specific to object-triggered action schemata and their selection, we employed a factorial design with two factors (RESPONSE: naming, pantomiming; and TRIGGER: pantomimes, objects) and four conditions (IA: imitating the observed pantomime; IO: pantomiming the use of the object shown; NA: naming the observed pantomime; NO: naming the object shown). This contrast between object-triggering of an action and imitation is somewhat analogous to the procedure used for different forms of grip by Grèzes et al. (2003). The design controls for the perceptual, semantic, lexical, and sensorimotor aspects of both object- and action-related processing. The experimental design specifically focuses at investigating the interaction [i.e. (IO−IA)−(NO−NA)] which allows the assessment of increased neural activity specific to the selection of action schemata triggered by objects.

Materials and methods

Subjects

Fourteen healthy right-handed males volunteers (mean age 26.14 ± 6.05 years) with no history of neurological or psychiatric illness gave informed consent. Handedness was assessed by the Edinburgh Inventory test (Oldfield, 1971). The study was approved by the ethics committee of the University Hospital of the RWTH—Aachen, Germany.

Experimental design and stimuli

A factorial design with the factors TRIGGER (objects and actions) and RESPONSE (pantomiming and naming) was employed. This results in four conditions: (i) IA, imitating the action observed; (ii) IO, pantomiming the use of the object shown; (iii) NA, naming the pantomime observed; and (iv) NO, naming the object shown. In the 'action performance' conditions, subjects were asked either to imitate the pantomime shown (IA) or to pantomime an action specific to the object shown (IO) with their right hand or arm. Like language, high-level motor control is a left-hemisphere cognitive ability so that when a lesion occurs in the left hemisphere, an apraxic deficit of both upper limbs is often observed in right-handed patients (De Renzi et al., 1968, 1982; Heilman, 1997; Liepmann, 1905). This implies that to study the neural basis of pantomiming and object use, it should be sufficient to test one hand. In the 'naming' conditions, subjects were asked to name either the pantomime (NA) or the object (NO) shown. Videotapes were used for displaying the triggers (pantomimes, objects) on a Video Display Unit (VDU) installed straight ahead of the subjects within reaching distance (eye-to-monitor distance 0.7 m; horizontal visual angle: 27°, vertical visual angle: 21°). The triggers (i.e. objects and pantomimes) were displayed with a visual angle of 18° in the vertical and horizontal plane. Object stimuli included manipulable items such as iron, toothpaste and jug, and tools such as screwdriver, bottle opener and paint roller. The pantomimes used as stimuli were movements that we would perform had we such objects and tools in hand. For each rCBF measurement, subjects first viewed a white screen for 15 s,

followed by the stimulus sequence which lasted 90 s. Each trigger was presented for 2.5 s followed by an inter-stimulus-interval (ISI) of 0.5 s. Thus, 30 stimuli were shown during each rCBF measurement. A black fixation cross was superimposed on the screen throughout the experiment to prevent differences in eye movements across the different conditions. Videotape recordings were performed online throughout the experimental sessions to monitor subjects' responses and thus allow for off-line performance analyses. For analysis of differential eye movements across conditions, eye movements were recorded during the rCBF measurements using an infrared device (iView-system SMI, Teltow, Germany).

PET hardware and procedures

Measurements of regional cerebral blood flow (rCBF) were taken using an ECAT HR+PET-scanner (CTI-Siemens) and ^{15}O-butanol using standard technology and procedures previously described in detail (see, e.g., Weiss et al., 2000, 2003). Subjects laid comfortably in the PET scanner. An intravenous cannula was placed in their left cubital vein for injection of the radioactive tracer. Twelve PET scans with three repeats per condition were carried out for each subject thus resulting in a total of 168 observations (12 rCBF scans per subject, 14 subjects). The order of rCBF measurements was counterbalanced within and across subjects.

Imaging processing and statistical analysis

Following standard image preprocessing (including image realignment, image normalization into standard stereotactic space, and smoothing), statistical analyses were performed using SPM99, (http://www.fil.ion.ucl.ac.uk/spm). For each pixel, across all subjects and all scans, the mean relative rCBF values were calculated separately for each of the main effects. Comparisons of the means were made using the *t* statistic and thereafter transformed into normally distributed *Z* statistics. The resulting set of *Z* values constituted a statistical parametric map ($SPM_{\{Z\}}$ map). For the contrasts of interest, the significance of these statistical parametric maps was assessed by comparing the expected and observed distribution of the *t* statistic under the null hypothesis of no differential activation effect on rCBF. Only activations that were significant at $P < 0.05$ (corrected for multiple comparisons across the entire brain volume) or better are reported.

Table 1
Local maxima of the areas of differentially increased neural activity associated with the main effect of PANTOMIMING

Region	Side	X	Y	Z	T
Pantomiming > naming					
(IA + IO > NA + NO)					
Motor cortex	L	−30	−22	66	24.1
Supplementary motor area	L	−6	−14	54	16.6
Cerebellum	R	20	−50	−24	11.4
Inferior parietal cortex (BA 40)	R	62	−30	28	9.8
Frontal operculum	R	48	2	8	5.7
	L	−44	−2	4	9.6
Dorsolateral prefrontal cortex	L	−34	34	30	7.6
Lateral ventral premotor cortex	R	56	8	20	5.0
	L	−54	6	30	6.2
Temporo-occipital junction (V5)	R	48	−58	14	5.0
	L	−56	−68	2	5.4
Putamen	L	−26	−4	6	5.0

Table 2
Local maxima of the areas of differentially increased neural activity associated with the main effect of NAMING

Region	Side	X	Y	Z	T
Naming > pantomiming					
(NA + NO > IA + IO)					
Motor cortex	R	54	−10	36	13.6
	L	−46	−12	30	13.1
Supplementary motor area	L	−2	16	64	8.7
Thalamus	R	8	−12	16	6.9
Anterior cingulate cortex	R	8	40	20	6.8
	L	−6	30	28	5.9
Inferior frontal gyrus	L	−44	24	4	7.7
Medial frontal gyrus	R	26	48	10	5.4
Superior frontal gyrus	L	−22	46	44	6.5
Lingual gyrus	R	24	−66	6	6.3
	L	−26	−48	−6	5.6
Temporo-occipital cortex	R	42	−88	18	6.5
Occipital cortex	L	−18	−102	−6	6.4
Cerebellar hemisphere	L	−18	−64	−22	6.6

The data were analyzed for the main factors TRIGGER (i.e. objects > pantomimes: IO + NO > IA + NA; pantomimes > objects IA + NA > IO + NO) and RESPONSE (i.e. naming > pantomiming: NA + NO > IA + IO; pantomiming > naming: IA + IO > NA + NO). Finally, as the experimental design aimed specifically at investigating the neural basis of the object-trigger system, we assessed the interaction terms [i.e. (IO−IA)−(NO−NA); (IA−IO)−(NA−NO)] which controls for the perceptual, motor, semantic, and language aspects of both object- and action-related processing.

For all statistical comparisons of interest, the stereotactic coordinates of the pixels of local maximum significant changes in relative rCBF within areas of significant relative rCBF change associated with the specific conditions were determined. The anatomical localization of these local maxima was assessed by reference to a standard stereotactic atlas (Talairach and Tournoux, 1988). Additional validation of this method of localization was obtained after superimposition of the $SPM_{\{Z\}}$ maps on the group mean MRI image calculated after each individual's MRI had been stereotactically transformed into the same standard stereotactic space.

Results

PET

Tables 1–4 show the local maxima of the areas of increased neural activity, as assessed by PET rCBF measurements, associated with the main effects. Analysis of the factor RESPONSE

Table 3
Local maxima of the areas of differentially increased neural activity associated with the main effect of OBJECTS

Region	Side	X	Y	Z	T
Objects > actions					
(NO + IO > NA + IA)					
Fusiform gyrus	R	32	−52	−14	5.9
	L	−28	−54	−14	9.8
Occipital cortex	R	30	−100	−4	6.7
	L	−36	−90	−6	7.1
Frontopolar cortex	L	−12	54	34	6.4

Table 4
Local maxima of the areas of increased neural activity associated with the main effect of ACTIONS

Region	Side	X	Y	Z	T
Actions > objects					
(NA + IA > NO + IO)					
Temporo-occipital junction (V5)	R	54	−62	6	18.3
	L	−46	−68	8	15.21
Primary visual cortex	R	6	−92	8	17.5
	L	−4	−94	10	15.3
Lateral dorsal premotor cortex	R	44	−2	48	7.1
	L	−50	−2	52	6.6

revealed the expected differential neural activations associated with pantomiming (relative to naming, Table 1) and with naming (relative to pantomiming, Table 2), respectively. Analysis of the factor TRIGGER revealed differential neural activations associated with object processing (relative to observing actions, Table 3) and with observing pantomimes (relative to object processing, Table 4), respectively. These activations replicate previous studies concerned with naming (Perani et al., 1999), motor task performance (Fink et al., 1997; Stephan et al., 1995), and object and

action recognition (Chao et al., 1999; Decety et al., 1997; Martin et al., 1995).

More importantly, with regard to the purpose of the study, selecting and producing a wide range of skilled actions triggered by objects (controlled for perceptual, motor, semantic, and lexical effects) specifically activated, as hypothesized, left inferior parietal cortex (dIPL, vIPL) as indicated by the interaction term (IO−IA)−(NO−NA) (Fig. 1). Additional areas of activation showing a significant interaction were observed in left dorsolateral prefrontal cortex (DLPFC), the left anterior cingulate cortex (ACC), and the left ventrolateral prefrontal cortex (VLPFC). Analysis of the corresponding rCBF plots shows clearly different patterns of neural responses for these areas (i.e. differential interaction patterns) which allow one to attribute the areas activated to differential cognitive processes (Fig. 1). Within left inferior parietal cortex, there is a more anterior and inferior region (labeled as vIPL) activated by both pantomiming conditions (IO and IA) to similar degrees (percentage signal change in condition IA 2.25 ± 0.75% versus condition IO 2.78 ± 1.46%; $P = 0.6$). This activation pattern suggests that this area is involved in object-related action performance irrespective of whether a pantomime was performed to an object or whether a pantomime was imitated. By contrast, the more dorsal and posterior
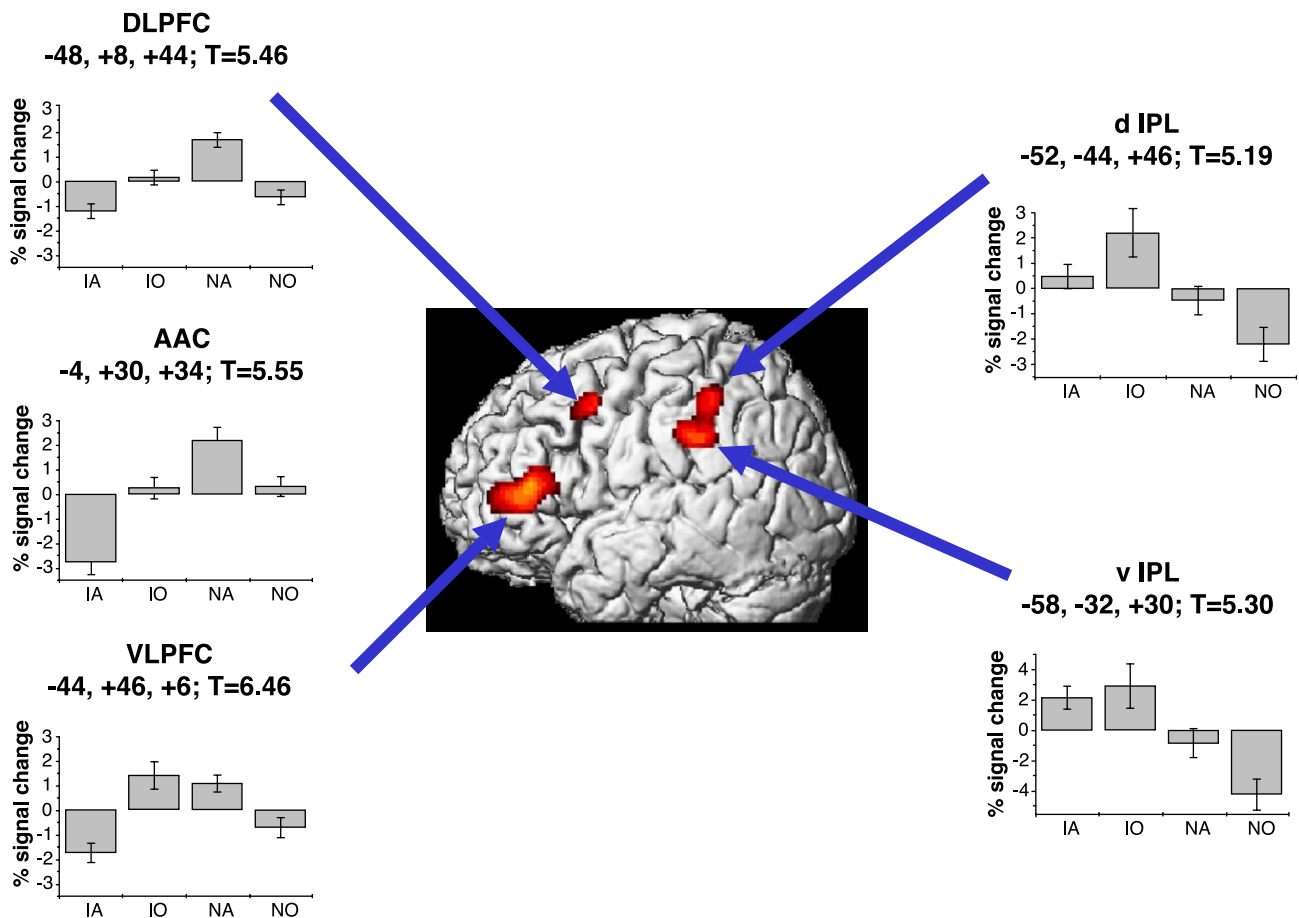

Fig. 1. Selecting and producing a wide range of skilled actions triggered by objects (controlling for perceptual, motor, semantic, and lexical processing) as assessed by the interaction term (IO−IA)−(NO−NA) activated the dorsal inferior parietal cortex [−52, −44, 46] ($t = 5.19$), the ventral inferior parietal cortex [−58, −32, 30] ($t = 5.30$), the ventrolateral prefrontal cortex [−44, 46, 6] ($t = 6.46$), the anterior cingulate cortex [−4, 30, 34] ($t = 5.55$), and the dorsal lateral prefrontal cortex [−48, 8, 44] ($t = 5.46$), all in the left hemisphere. The plots of the percentage of rCBF-signal change associated with the activated areas are displayed clockwise starting from the up right position.
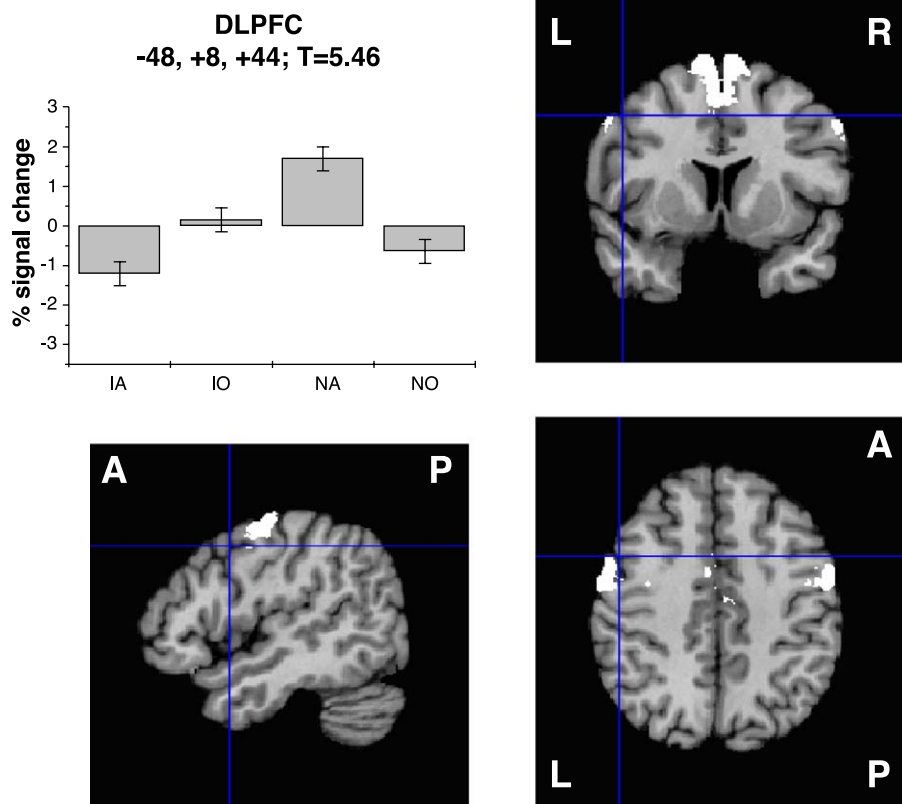
Fig. 2. Position of the maximally activated voxel (−48, +8, +44, blue crosshairs) within the activation revealed by the interaction term, which was in the dorsolateral frontal cortex, in respect to a cytoarchitectonically defined probability map of the premotor cortex (i.e. Brodmann area 6, white shading). A= anterior, P = posterior, L= left, R= right.

activation in left inferior parietal cortex (labeled as dIPL), an area that has not previously been selectively activated, is specific to pantomiming condition when objects triggered the action. This rCBF response pattern suggests that this area is the locus of the trigger system (percentage signal change in condition IA $0.47 \pm 0.48\%$ versus condition IO $2.20 \pm 0.95\%$; $P < 0.001$).

There were three activations sites in the anterior part of the left hemisphere (Fig. 1). The VLPFC was most active in the two tasks with different inputs and different outputs, namely, the pantomime of object use (IO) and the naming of pantomimes (NA). In contrast, the left dorsolateral frontal cortex and the anterior cingulate cortex (ACC) were more active when subjects named pantomimes (NA). Since the DLPFC and the premotor cortex have a common (lateral) border, we assessed whether the dorsolateral frontal activation was located indeed within the DLPFC or within the premotor cortex (i.e. Brodmann area 6). For this purpose, we determined the position of the local maximum, that is, the coordinates of the maximally activated voxel within this activation (−48, +8, +44), with respect to a cytoarchitectonically defined probability map of the premotor cortex (i.e. Brodmann area 6; Geyer et al., 2001). Fig. 2 clearly shows that the local maximum lies anterior to Brodmann area 6. Furthermore, the rCBF plot (see Fig. 2) shows specific activation of the maximally activated voxel within this activation of the interaction term in the condition NA (naming pantomime), which strongly implies that the observed area of activation is prefrontal [as a premotor activation would be expected to show up in both conditions requiring motor responses (imitation of pantomime, IA, and pantomiming of object use, IO)].

The analysis of the second interaction term, that is, from the imitation perspective (IA−IO)−(NA−NO), led to no significant activation.

Behavioral data

Pantomime and naming performances were scored by three independent judges. Since there were no differences among judges' scores, two different ANOVAs for repeated measures with Task (IA, IO or NA, NO) and Repeat (1, 2, 3) as factors were applied to the averaged action and naming scores, respectively. Fig. 3 plots the subjects' mean scores for the performance in the four tasks averaged across the three repeats. As for actions, both the main
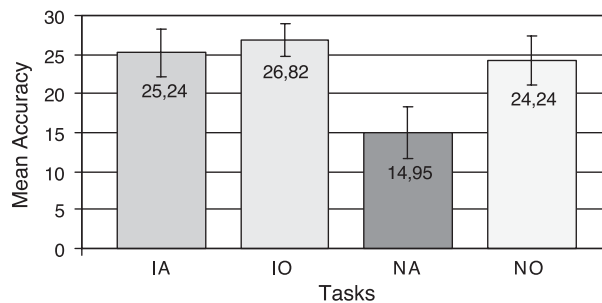

Fig. 3. The graph plots the mean of subjects' correct responses for the four different tasks (IA, IO, NA, NO). For each subject, the value is averaged across three repeats (max = 30). The bars indicate the standard deviations.

effects of Task [$F(1)$= 16.73, $P < 0.001$] and Repeat [$F(2)$= 8,042, $P < 0.002$] were significant but not the interaction. The results suggest that subjects found it more difficult to imitate pantomimes (mean accuracy in performing the IA condition 25.24 ± 3.06, 84%, for $n = 30$) than to pantomime the use of objects (mean accuracy in performing the IO condition, 26.82 ± 2.11, 89%), and that their performance improved across repeats. In particular, there was a significant difference between subjects' performance in repeats 1 and 2, and 1 and 3 when they imitated pantomimes, and only between repeats 1 and 3 when they pantomimed the use of objects (all $P < 0.05$). With regard to naming, the only significant result was the main effect of Task [$F(1)$= 16.73, $P < 0.001$] indicating that naming pantomimes (mean accuracy in performing the NA condition 14.95 ± 3.31, 50%) was more effortful than naming objects (mean accuracy in performing the NO condition 24.24 ± 3.10, 81%).

Eye movements

As far as eye movement data are concerned, the analysis showed no significant differential eye movements across the conditions: subjects were able to maintain fixation throughout all conditions.

Discussion

The main purpose of this study was to establish the neural basis of pantomiming object and tool use in the normal human brain. We employed a pantomiming task as it predicts well actual object and tool use (De Renzi and Lucchelli, 1988; Goldenberg and Hagmann, 1998) but it is easier to implement in a PET scanning environment. Our data extend previous imaging and neuropsychological data by allowing a specification of the areas sustaining the production of object-related pantomimes. The analysis of the rCBF data associated specifically with each condition allows us to assign differential contributions of the areas activated to specific cognitive aspects of task performance. The key result is the identification of a region in the more dorsal part of inferior parietal cortex which is specifically activated when objects trigger pantomimes. We argue that this area is the specific anatomical correlate for the system triggering object-related action schemata in humans. This region when lesioned—or disconnected from more anterior areas—may lead to the selective deficit shown by apraxic patients who experience impaired everyday use of objects: ideational apraxia (De Renzi and Lucchelli, 1988; De Renzi et al., 1968; Liepmann, 1905; Rumiati et al., 2001). A deficit in pantomiming the use of visually presented objects is often seen in association with apraxia of object use although there is evidence that these two deficits may dissociate (Kato et al., 2001). A double dissociation between object use and pantomiming on verbal command is also reported (Motomura and Yamadori, 1994; Watson et al., 1986).

This region is much less activated by object naming. The claim that the triggering system is independent of a system concerned with semantic attributes of objects is also supported by neuropsychological evidence. Apraxic patients with parietal lesions have been described who are able to identify correctly and to show good knowledge of objects they misuse (Rumiati et al., 2001); conversely, patients with temporal atrophy and semantic dementia efficiently manipulate objects and tools

although they retain little linguistic and semantic knowledge (Buxbaum et al., 1997; Lauro-Grotto et al., 1997).

A second area showing an activation in the interaction analysis in our study was the ventral inferior parietal cortex. It is close to some of the activation sites reported previously in ventral parietal cortex in association with tool use and in particular with grasping (Binkofski et al., 1999; Grafton et al., 1996a; Grefkes et al., 2002). The activation of the ventral parietal cortex in our study may thus be related to the human equivalent of macaque area AIP. Previous imaging work, employing less complex tasks such as grasping (Grafton et al., 1996a) or using limited sets of basic meaningful and meaningless objects (Binkofski et al., 1999), has shown the involvement of a network of areas including the anterior parietal cortex in praxis. Likewise, electrophysiological activation underlying grasp movements has been found in a specific area along the anterior aspect of the intraparietal sulcus in the macaque, namely, anterior intraparietal area AIP (Sakata et al., 1995; Taira et al., 1990). Macaque area AIP contains neurons sensitive to three-dimensional features of objects such as shape, orientation, and size (Sakata et al., 1995; Taira et al., 1990), which could indicate that these precursors in the monkey may have constituted the bases for the development of much more complex object-related action schemata in man. The most direct test of the existence of AIP in humans, as it uses stimuli corresponding to those employed in the monkey, is that of Grefkes et al. (2002). The location of the activation in that study is in the anterior aspect of the human intraparietal sulcus in its depth on the lateral bank. The local maximum of the activation observed in the interaction analysis of the current study is more on the lateral surface of the inferior parietal cortex, held by Brodmann to be a specifically human structure. Although differences in the exact localizations of the respective peaks of activation in the two studies may also be ascribed to the fact that fMRI and PET, respectively, were used, these results suggest that the evolutionary development of our repertoire of skilled actions has led to the colonization of cortical regions adjacent to those which are concerned with the elicitation of grasp movements. This is an analogous relation to that suggested for temporal cortex on the relation between movement and action recognition by Martin and Chao (2001). Recent neurophysiological and neuroanatomical studies have clarified that the parietal lobe in monkey consists of a multiplicity of areas with specific connections to the premotor cortex. Together, these areas mediate distinct sensorimotor transformations related to the control of hand, arm, eye, or head movements (for a review, see Rizzolatti et al., 2002; Rizzolatti and Luppino, 2001) and in particular, eye–hand coordination during reaching (Marconi et al., 2001).

If we turn to the more anterior activation sites, an interaction was shown in the left DLPFC and the left ACC. Interestingly, the rCBF plots of these activation sites seem to parallel the task difficulty of the respective conditions as assessed by the error rates. Why, however, should naming pantomimes be particularly difficult? Allport and Wiley (2000) have shown that when different tasks involve the same stimuli within a single session, task sets inappropriate at a particular time need to be inhibited. One possibility is that the activation observed in the DLPFC is just anterior of the sites of grip elicitation by objects observed by Grèzes et al. (2003). The activation observed may thus be related to the need to suppress an inappropriate but dominant response, that

is, imitating the action observed rather than naming it to correspond adequately to the task instructions (Fink et al., 1999).

As far as the VLPFC was concerned, the area was most active when subjects pantomimed the object use (IO) and named actions (NA). If one examines the naming task, then there is a large swathe of VLPFC activation where action naming is significantly more activated ($t = 9.2$) than object naming. More dorsally, there is a region which for the two object presentation tasks is significantly more activated ($t = 6.5$) when an action has to be produced rather than named. The significant interaction may thus just correspond to the overlap between two graded regions as that occurring in processing of spatial and object information in prefrontal cortex (Courtney et al., 1998). An alternative possibility is that these two tasks are the ones that differentially require action semantics (Lauro-Grotto et al., 1997).

In summary, our findings suggest that there is a close link between seen objects and tools and the information associated with their use. In right-handed individuals, the key brain structure for an object system that triggers actions is in the dorsal inferior parietal cortex of the left hemisphere, as this was the most activated area when subjects pantomimed the use of objects and tools. The findings reported here are in good accordance with neuropsychological data of apraxic patients and provide an explanation for why left parietal damage may result in impaired tool use (and impaired pantomiming of tool use) despite intact semantic and linguistic functions.

Acknowledgments

References

Allport, D.A., Wylie, G., 2000. Task switching, stimulus-response binding, and negative priming. In: Monsell, S., Driver, J. (Eds.), Control of Cognitive Processes: Attention and Performance, vol. XVIII. MIT Press, Cambridge, MA, pp. 35–70.

Binkofski, F., Buccino, G., Stephan, K.M., Rizzolatti, G., Seitz, R.J., Freund, H.J., 1999. A parieto-premotor network for object manipulation: evidence from neuroimaging. Exp. Brain Res. 128, 210–213.

Buxbaum, L.J., Schwartz, M.F., Carew, T.G., 1997. The role of semantic memory in object use. Cogn. Neuropsychol. 14, 219–254.

Byrne, R.W., 2002. Seeing actions as hierarchically organized structures. Great ape manual skills. In: Meltzoff, A., Prinz, W. (Eds.), The Imitative Mind: Development, Evolution, and Brain Bases. Cambridge Univ. Press, Cambridge, pp. 122–140.

Chao, L.L., Haxby, J.V., Martin, A., 1999. Attribute-based neural substrates in posterior temporal cortex for perceiving and knowing about objects. Nat. Neurosci. 2, 913–919.

Cooper, R., Shallice, T., 2000. Contention scheduling and the control of routine activities. Cogn. Neuropsychol. 17, 297–338.

Courtney, S.M., Petit, L., Maisog, J.M., Ungerleider, L.G., Haxby, J.V., 1998. An area specialized for spatial working memory in human frontal cortex. Science 279, 1347–1351.

De Renzi, E., Barbieri, C., 1992. The incidence of the grasp reflex following hemispheric lesion and its relation to frontal damage. Brain 115, 293–313.

De Renzi, E., Lucchelli, F., 1988. Ideational apraxia. Brain 111, 1173–1185.

De Renzi, E., Pieczuro, A., Vignolo, L.A., 1968. Ideational apraxia: a quantitative study. Neuropsychologia 6, 41–52.

De Renzi, E., Faglioni, P., Sorgato, P., 1982. Modality-specific and supramodal mechanisms of apraxia. Brain 105, 301–312.

Decety, J., Perani, D., Jeannerod, M., Bettinardi, V., Tadary, B., Woods, R., Mazziotta, J.C., Fazio, F., 1994. Mapping motor representations with positron emission tomography. Nature 371, 45–52.

Decety, J., Grezes, J., Costes, N., Perani, D., Jeannerod, M., Procyk, E., Grassi, F., Fazio, F., 1997. Brain activity during observation of actions: influence of action content and of subject's strategy. Brain 120, 1763–1777.

Fink, G.R., Frackowiak, R.S., Pietrzyk, U., Passinsham, R.E., 1997. Multiple nonprimary motor areas in the human cortex. J. Neurophysiol. 77, 2164.

Fink, G.R., Marshall, J.C., Halligan, P.W., Frith, C.D., Driver, J., Frackowiak, R.S., Dolan, R.J., 1999. The neural consequences of conflict between intention and the senses. Brain 112, 497–512.

Geyer, S., Grefkes, C., Schormann, T., Mohlberg, H., Zilles, K., 2001. The microstructural border between the agranular frontal (Brodmann's area 6) and the granular prefrontal cortex A population map in standard anatomical format. NeuroImage 13, S1171.

Gibson, J.J., 1979. The Ecological Approach to Perception. Houghton Mifflin, Boston.

Goldenberg, G., Hagmann, S., 1998. Tool use and mechanical problem solving in apraxia. Neuropsychologia 36, 581–598.

Grafton, S.T., Fagg, A.H., Woods, R.P., Arbib, M.A., 1996a. Functional anatomy of pointing and grasping in humans. Cereb. Cortex 6, 226–237.

Grafton, S.T., Arbib, M.A., Fadiga, L., Rizzolatti, G., 1996b. Location of grasping representation in humans by positron emission tomography: 2. Observation compared to imagination. Exp. Brain Res. 112, 103–111.

Grefkes, C., Weiss, P.H., Zilles, K., Fink, G.R., 2002. Crossmodal processing of object features in human anterior intraparietal cortex: an fMRI study implies equivalences between humans and monkeys. Neuron 35, 173–184.

Grèzes, J., Decety, J., 2002. Does visual perception of object afford action? Evidence from a neuroimaging study. Neuropsychologia 2, 212–222.

Grèzes, J., Armony, J.L., Rowe, J., Passingham, R.E., et al., 2003. Activations related to "mirror" and "canonical" neurones in the human brain: an fMRI study. NeuroImage 18, 928–937.

Heilman, K.M., 1997. Handedness. In: Gonzales Rothi, L.J., Heilman, (Eds.), Apraxia: the Neuropsychology of Action. Psychology Press, Hove, pp. 19–28.

Humphreys, G.W., Riddoch, M.J., 2002. Detection by action: neuropsychological evidence for action-defined templates in search. Nat. Neurosci. 4, 84–88.

Jenkins, I.H., Brooks, D.J., Nixon, P.D., Frackowiak, R.S.J., Passingham, R.E., 1994. Motor sequence learning: a study with positron emission tomography. J. Neurosci. 14, 3775–3790.

Kato, M., Meguro, K., Sato, M., Shimada, Y., Yamazaki, H., Saito, H., Yamaguchi, S., Yamadory, A., 2001. Neuropsychiatry Neuropsychol. Behav. Neurol. 14, 45–52.

Lauro-Grotto, R., Piccini, C., Shallice, T., 1997. Modality-specific operations in semantic dementia. Cortex 33, 593–622.

Lehmkuhl, G., Poeck, K., 1981. A disturbance in the conceptual organization of actions in patients with ideational apraxia. Cortex 17, 153–158.

Lhermitte, F., 1983. Utilization behavior and its relation to lesion of the frontal lobes. Brain 106, 237–255.

Liepmann, H., 1905. Die linke Hemisphere und das Handeln. Münchner medizinische Wochenschrift 49, 2322–2326, 2375–2378.

Marconi, B., Genovesio, A., Battaglia-Mayer, A., Ferraina, S., Squatrito, S., Molinari, M., Laquaniti, F., Caminiti, R., 2001. Eye-hand coordi-

nation during reaching. I. Anatomical relationships between parietal and frontal cortex. Cereb. Cortex 11, 513–527.

Marshall, J.C., Fink, G.R., 2003. Cerebral localization: then and now. NeuroImage 20 Suppl. 1, S2–S7.

Martin, A., Chao, L.L., 2001. Semantic memory and the brain: structure and processes. Curr. Opin. Neurobiol. 11, 194–201 (Review).

Martin, A., Wiggs, C.L., Ungerleider, L.G., Haxby, J.V., 1995. Neural correlates of category-specific knowledge. Nature 379, 649–652.

McGrew, W.C., 1993. The intelligent use of tools: twenty propositions. In: Gibson, K.R., Ingold, T. (Eds.), Tools, Language and Cognition in Human Evolution. Cambridge Univ. Press, Cambridge, pp. 151–170.

McLeod, P., 1987. Visual reaction time and high-speed ball games. Perception 16, 45–49.

Motomura, N., Yamadori, A., 1994. A case of ideational apraxia with impairment of object use and preservation of object pantomime. Cortex 30, 167–170.

Norman, D.A., Shallice, T. 1980. Attention to action: willed and automatic control of behaviour. Center for human information processing (Technical Report No.99) (Reprinted in revised form in: Davidson, R.J., Schwartz, G.E., Shapiro, D. Eds., Consciousness and self regulation, vol. 4, Plenum, New York).

Oldfield, E., 1971. The assessment and analysis of handedness: the Edinburgh Inventory. Neuropsychologia 9, 97–113.

Perani, D., Cappa, S.F., Schnur, T., Tettamanti, M., Collina, S., Rosa, M.M., Fazio, F., 1999. The neural correlates of verb and noun processing. A PET study. Brain 122, 1344–2337.

Riddoch, M.J., Humphreys, G.W., 1998. Visual affordances direct action: neuropsychological evidence from manual interference. Cogn. Neuropsychol. 15, 645–683.

Rizzolatti, G., Luppino, L., 2001. The cortical motor system. Neuron 31, 889–901.

Rizzolatti, G., Fogassi, L., Gallese, V., 1997. Parietal cortex: from sight to action. Curr. Opin. Neurobiol. 7, 562–567.

Rizzolatti, G., Fogassi, L., Gallese, V., 2002. Motor and cognitive functions of the ventral premotor cortex. Curr. Opin. Neurobiol. 12, 149–154.

Rumiati, R.I., Humphreys, G.W., 1998. Recognition by action: dissociating visual and semantic routes to actions in normal observers. J. Exp. Psychol. Hum. Percept. Perform. 2, 631–647.

Rumiati, R.I., Zanini, S., Vorano, L., Shallice, T., 2001. A form of ideational apraxia as a deficit of contention scheduling. Cogn. Neuropsychol. 18, 617–642.

Sakata, H., Taira, M., Murata, A., Mine, S., 1995. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. Cereb. Cortex 5, 429–438.

Shallice, T., Burgess, P.W., Schon, F., Baxter, D.M., 1989. The origins of utilization behavior. Brain 112, 1587–1598.

Stephan, K.M., Fink, G.R., Passingham, R.E., Silbersweig, D., Ceballos-Baumann, A.O., Frith, C.D., Frackowiak, R.S., 1995. Functional anatomy of the mental representation of the upper extremity movements in healthy subjects. J. Neurophysiol. 723, 373–386.

Taira, M., Mine, S., Georgopoulos, A.P., Murata, A., Sakata, H., 1990. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. Exp. Brain Res. 83, 29–36.

Talairach, J., Tournoux, P., 1988. Co-Planner Stereotaxic Atlas of the Human Brain. Thieme, Stuttgart.

Tucker, M., Ellis, R., 1998. On the relations between seen objects and components of potential actions. J. Exp. Psychol. Hum. Percept. Perform. 24, 830–846.

Watson, R.T., Fleet, W.S., Gonzales-Rothi, L., Heilman, K.M., 1986. Apraxia and the supplementary motor area. Arch. Neurol. 43, 787–792.

Weiss, P.H., Marshall, J.C., Wunderlich, G., Tellmann, L., Halligan, P.W., Freund, H.J., Zilles, K., Fink, G.R., 2000. Neural consequences of acting in near versus far space: a physiological basis for clinical dissociations. Brain 123, 2531–2541.

Weiss, P.H., Marshall, J.C., Zilles, K., Fink, G.R., 2003. Are action and perception in near and far space additive or interactive factors? NeuroImage 18, 837–846.

Wolpert, D.M., Ghahramani, Z., 2000. Computational principles of movement neuroscience. Nat. Neurosci. 3, 1212–1217.