Pantomime of Tool Use Depends on Integrity of Left Inferior Frontal Cortex

Pantomime of tool use is a frequently used test for apraxia. For basic cognitive neuroscience, pantomime of tool use is of interest because it constitutes a link between instrumental and communicative manual actions. We used lesion subtraction analysis to determine the locations specifically associated with defective pantomime of tool use in patients with left-brain damage and aphasia. Subtraction of lesions of patients with normal pantomime from those with defective pantomime yielded a maximum difference in the inferior frontal gyrus and adjacent portions of the insula and precentral gyrus. This result remained essentially the same when possible confounding influences of impaired language comprehension and of lesion size were controlled by selecting patients equated on these measures and when only patients with preserved imitation of gestures were considered. By contrast, parietal lesions did not have a specific impact on pantomime. We speculate that the vulnerability of pantomime to lesions of left inferior frontal cortex is due to the high demands on selection of a very restrained range of features out of the many features that may come to mind when imagining the actual use of the tool.

Keywords: apraxia, frontal lobe, pantomime, parietal lobe, tool use

Introduction

For testing pantomime of tool use, subjects are requested to shape their hand as if it would hold a tool and perform the movements they would make when actually applying that tool. Pantomime of tool use is a traditional test in clinical neuropsychology and neuropsychology (Lieberman 1908; Goodglass and Kaplan 1963; Geschwind 1975; Barbieri and De Renzi 1988; Roy and Hall 1992; Heilman and Rothi 1993; Goldenberg et al. 2003), which has recently moved into the focus of cognitive neuroscience. Pantomime of tool use depends on command. The aim of the present study was to elucidate the location of left-brain lesions impairing pantomime independently from their effect on imitation of gestures.

Methods

Participants

Forty-four patients admitted to the ward or the day care clinics of the Neuropsychological Department of Bogenhausen Hospital were included. Right-handed patients who had aphasia caused by a first left-sided cerebrovascular accident at least 3 weeks before were examined. Patients were excluded when no magnetic resonance imaging (MRI) could be obtained or when the MRI revealed bilateral or diffuse lesions. All patients had a complete Aachen aphasia test (AAT) (Huber et al. 1983) within 14 days from the experimental tests. The patients or their relatives gave their informed consent for participation in the study, which was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Demographic and clinical data are provided in Table 1.
Pantomime of Tool Use

Patients were asked to mime the use of 20 common tools or objects. The examiner named the action and the object and simultaneously showed a photograph of the object. This photograph was hidden from view before subjects started miming.

Patients were asked to respond with the ipsilesional left hand when restricted motility of the right hand interfered with the exactitude of the pantomime. For evaluation, the examiner marked the presence or absence of predefined features of the pantomime on an examination sheet. For each item, 1 feature characterized grip and finger configuration, whereas the remaining 1–3 features concerned position and movement of the whole hand (e.g., screwing in of an electric bulb: spherical grip and rotation of the hand; cutting with scissors: bended fingers with opposition of thumb, opening and closing of hand or fingers, hand oriented perpendicularly to table, and movement of whole hand parallel to table—see Supplementary Material for complete scoring sheet). Summed up across all 20 items, there were 55 features.

This task is a slightly adapted version of the task used by Goldenberg et al. (2003). Interrater agreement for scoring had been found very satisfactorily with the previous version for the number of correct features per item (kappa = 0.61, P < 0.0001) as well as for the total score summed up across all items (r = 0.94, P < 0.00001). Normative data for the new version were obtained from 49 healthy controls (25 female, 24 male; mean age 49, standard deviation [SD] 11.4). Pantomime was considered as defective when the score was below the fifth percentile of this control group (14/55—see Supplementary Material for distribution of control scores).

Imitation of Meaningless Gestures

Meaningless gestures were preferred for testing imitation because imitation of meaningful gestures, like, for example, the pantomimes of tool use, can be achieved by comprehension of the gesture’s meaning and subsequent reproduction of a gesture with the same meaning out of long-term memory. By contrast, imitation of meaningless gestures compels to genuine imitation of the gesture’s shape (Goldenberg and Hagmann 1997; Tesserai and Rumiai 2004). Two variants of meaningless gestures were tested: 10 hand postures required the patients to copy different positions of the hand relative to the head and face while the configuration of the fingers remained invariant. For imitation of 10 finger postures, patients were asked to replicate different configurations of the fingers. The position of the whole hand relative to the body was not considered for scoring (see Supplementary Material for scoring sheet with illustration of all postures).

All patients imitated with their left arm and hand while the examiner demonstrated the gestures “like a mirror” with his right hand. The patients were allowed to start imitation as soon as the demonstration was terminated. For correct imitation on first trial, 2 points were credited. Otherwise, the demonstration was repeated and 1 point was given for a successful second trial. Scoring considered only the final position of the relevant body part and did not take into account hesitation, searching movements, or self-corrections during the course of the movement. In a previous study using the same test, interrater agreement of scoring 92% for hand and 99% for finger gestures (Goldenberg and Strauss 2002) was seen.

For determination of cutoff scores, we used previously published data obtained by administration of the same test to 60 healthy controls (23 female, 37 male, mean age 54.4, SD 14.0; Goldenberg 1996). Imitation was classified as disturbed when either hand or finger postures were below the fifth percentile of the control group (18/20 for hand, 17/20 for fingers—see Supplementary Material for distribution of control scores).

Lesion Analysis

MRI scans were obtained at the Bogenhausen Hospital’s radiological service on a 1.0-T MR system (MagNavi, Siemens, Erlangen, Germany). The T1 sequence used for analysis of lesion location was acquired with 19 axial slices (thickness 5 mm; interslice gap 1.5 mm), a field of view of 201 × 230 mm², matrix 224 × 512, a repetition time of 3600 ms, and an echo time of 96 ms. The minimum time between stroke and imaging was 3 weeks; the average period for the 44 patients was 16.4 weeks (SD 17.0 weeks).

Mapping of lesions was carried out by one experimenter (H.-O.K.) without knowledge of test results and clinical features of the patients. Lesions were mapped using MRicro software (Rorden and Brett 2000; http://www.sph.sc.edu/comd/rorden/) on slices of a T1-weighted template MRI scan from the Montreal Neurological Institute (http://www.bic.mni.mcgill.ca/cgi/icbview). This template is approximately distributed with MRIcro. The template scan provides various anatomical landmarks for precisely plotting size and localization of the lesion. Lesions were mapped onto the slices that correspond to z coordinates by using the identical or the closest matching transversal slices of each individual.

To identify the structures that are commonly damaged in patients with defective pantomime, we subtracted the superimposed lesions of patients scoring within the control range from those scoring below the cutoff score. Because there were less unimpaired than impaired patients, we used proportional values for the MRicro subtraction analysis, which consequently yielded a percentage overlay plot (for details concerning the subtraction technique, see Rorden and Karnath 2004). Automatic 3-dimensional rendering of the lesion data was carried out using MRicro.

Results

In the entire group of 44 patients, pantomime of tool use was defective in 29 patients and within the normal range in 15 (Table 1). The accuracy of grip and finger configuration was tightly related to the accuracy of hand position and movement in patients with defective pantomime (r = 0.76, P < 0.0005), but not in those who scored within the normal range (r = 0.33).

Table 1 compares demographic and clinical data as well as lesion size between patients with defective and normal pantomime. Differences were evaluated by chi square- or t-test. There were no differences of age, gender, time since lesion, etiology, or hand used. Patients with defective pantomime had significantly larger lesions, and greater severity of aphasia was reflected in lower scores on all AAT subtests. The distribution of aphasia types differed. The proportion of global aphasia was higher (P < 0.01) and that of Wernicke aphasia was lower (P < 0.05) in patients with defective pantomime than in those with...
normal pantomime. Finally, imitation of finger but not of hand postures was poorer in patients with defective pantomime.

**Lesion Subtraction: Defective versus Normal Pantomime**

Figure 1 shows the subtraction of lesions of patients with normal pantomime from those with defective pantomime. The highest difference of lesion density between patients with defective and those with normal pantomime was found in the opercular part of the inferior frontal gyrus (IFG), adjacent portions of the insula and of the precentral gyrus, and white matter below the precentral gyrus.

**Lesion Subtraction with Control for Lesion Size and Language Comprehension**

Table 1 shows that patients with defective and with normal pantomime differed not only in their ability to mime tool use but also in lesion size, severity of aphasia, and imitation of finger postures. In a second step of analysis, we controlled for possible influences of lesion size and language disturbance on lesion location by exclusion of patients with extreme values on these variables. We choose the AAT subtest language comprehension as the primary target for equating severity of aphasia because insufficient comprehension of verbal instructions is more likely to have an influence on the nonverbal task of producing pantomimes than the linguistic abilities assessed by the other AAT subtests. There were 5 patients with defective pantomime whose scores on language comprehension were lower than the minimum score of patients with normal pantomime and 4 patients with normal pantomime whose comprehension scores were higher than the maximum score of patients with defective pantomime. These patients were discarded from the following analysis. Furthermore, we excluded the 5 patients with defective pantomime who had the largest lesions and the 3 with normal pantomime who had the smallest lesions. As 1 patient with normal pantomime fulfilled both criteria, the total number of excluded patients was 6 for normal and 10 for defective pantomime. Demographic and clinical data of the remaining 28 patients are displayed in Table 2.

Comparison of lesion size and language comprehension between the remaining patients with defective versus normal pantomime revealed no significant differences (t-test; lesion size: \( P = 0.10 \); comprehension: \( P = 0.51 \)). Of the other clinical and demographic variables, only differences of naming and of imitation of finger postures came close to conventional significance levels (both \( P = 0.07 \)). All other comparisons yielded significance levels of \( P > 0.2 \).

Figure 2a shows the result of subtraction of patients with normal pantomime from those with impaired pantomime. Impaired pantomime was associated with higher density of lesion overlap in the IFG, insula, and pre- and postcentral gyri.

**Lesions Causing Defective Pantomime in Patients with Preserved Imitation**

To exclude any potential influences of impaired imitation on the pattern of lesion location associated with defective pantomime and to highlight only locations exclusively related to pantomime, we conducted a third subtraction analysis considering only patients with normal imitation. Of 11 patients who imitated both hand and finger postures within the normal range, 6 showed defective and 5 normal pantomime. Demographic and clinical data of these patients are displayed in Table 3.

The remaining groups did not significantly differ on any demographic or clinical measure (t-test or Fisher’s exact test, all \( P > 0.2 \)) except pantomime, but it is remarkable that there was no patient with global or Broca aphasia and normal pantomime and no patient with Wernicke aphasia and defective pantomime. Figure 2b shows the result of lesion subtraction. The maximum differences between lesions associated with defective versus normal pantomime were located in the IFG, the insula, putamen, superior temporal gyrus, the pre- and postcentral gyri, and white matter underlying the central gyri.

**Discussion**

We analyzed the location of lesions causing defective pantomime of tool use in 3 steps with increasingly stringent control for possible confounding variables. Analysis of unselected patients provided a large sample size but did not control for the possible influences of confounding variables. Tightening of selection criteria led to a decrease of sample size, which carries a risk of overrating anatomical variation in individual patients. However, consistent findings across the different comparisons pointed to reliable results: All 3 analyses agreed that pantomime of tool use depends on integrity of the IFG and adjacent portions of the insula and the precentral gyrus.

The area of lesion overlap further extended into the underlying white matter. Thus, it is possible that damage of projections to or from cortical areas contributed to pantomime disturbance (Lieberman 1905; Geschwind 1975; Catani and ffytche 2005). Future studies using diffusion tensor tractography and magnetic resonance perfusion techniques will be necessary to clarify the possible role of fiber tract lesions for pantomime of tool use.

Our analysis demonstrates regions that are damaged more frequently in patients with defective pantomime than in patients who likewise have brain damage but do not show the disorder (Rorden and Karnath 2004). As any analysis based on group comparisons, it does not exclude the possibility of defective pantomime in single patients with lesions in other regions. Nevertheless, our finding that frontal but not parietal regions are crucial for intact pantomime is difficult to reconcile with the proposal that the parietal lobe stores representations for actual tool use as well as for the demonstration of tool use by pantomime (Heilman et al. 1982; Buxbaum et al. 2005). Our failure to find an influence of parietal lesions on pantomime is unlikely to be due to a general underrepresentation of such lesions in our patient sample. In a companion study (Goldenberg and Karnath 2006), we examined the same group of patients in order to determine the location of lesions impairing the imitation of hand and finger postures. That analysis revealed a predominance of inferior parietal lesions in patients with defective imitation of hand postures. The conclusion that left parietal lesions affect imitation of gestures but not pantomime is corroborated by single case reports of patients with left parietal lesions who had severe difficulties with imitation of meaningless gestures but could produce pantomimes perfectly (Mehler 1987; Goldenberg and Hagmann 1997; Peigneux et al. 2000).

The absence of a prominent effect of parietal lesions on pantomime appears at odds with recent functional imaging studies, which consistently showed left parietal activation when neurologically healthy individuals mime the use of tools (Moll et al. 2000; Choi et al. 2001; Rumia et al. 2004; Ohgami et al. 2005).
For these studies, subjects were lying in a scanner without visual feedback from their manual action and the space surrounding it. Furthermore, to avoid head movements, they were not allowed to move the arm at the shoulder and consequently had to perform all gestures within the space between chest and waist. These restrictions afford a transposition of movement trajectories into a reference frame centered on the supine trunk of the own body, whereas in clinical testing and in gestural communication, actions are directed toward other body parts—for example, the mouth and face in tooth brushing or drinking—or are constructed with reference to the basic coordinates of external space, which are indicated by horizontal and vertical surfaces of surrounding objects. Parietal
Activation could be related to such additional demands on body-centered spatial transformations (Bonda et al. 1995; Alivisatos and Petrides 1997; Felician et al. 2004; Goldenberg and Karnath 2006). A further difference that possibly influences the weight given to the contributions of different brain regions concerns the timing of pantomimes. In the functional imaging studies, the time for 1 pantomime ranged from 2 to 6 s. In contrast, evaluation of video-recorded tests showed that aphasic patients frequently needed more than 10 s for completion of a pantomime. It may be speculated that the fast pace of testing in functional magnetic resonance imaging (fMRI) studies highlighted the activity of regions whose contributions can be replaced by compensatory mechanisms when pantomimes are produced without time limits.

However, both our research and the functional imaging studies convergently suggest a prominent role of the left IFG and adjacent portion of the insula and the precentral gyrus for pantomime. With the exception of 2 early studies (Moll et al. 2000; Choi et al. 2001), all subsequent fMRI studies of pantomime in normal subjects documented activations of left prefrontal and frontal opercular regions largely overlapping with the regions whose integrity we found to be essential for correct pantomime (Rumiati et al. 2004; Ohgami et al. 2004; Johnson-Frey et al. 2005; Fridman et al. 2006; Hermsdorf et al. forthcoming). Our lesion study demonstrates that activity within these areas is not only correlated with but also necessary for pantomime of tool use.

Ventral premotor cortex and the opercular portion of IFG have been proposed to be the repository of a “vocabulary” of motor actions (Binkowski et al. 2000; Rizzolatti and Luppino 2001), which serves for translating information about object properties and action goals into combinations of motor programs.

Table 2
Demographic and clinical data of patient groups equated for lesion size and language comprehension

<table>
<thead>
<tr>
<th></th>
<th>Pantomime defective</th>
<th>Pantomime normal</th>
</tr>
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<tbody>
<tr>
<td>Female/male</td>
<td>10/9</td>
<td>5/4</td>
</tr>
<tr>
<td>Age</td>
<td>53.4 (15.4)</td>
<td>53.8 (12.1)</td>
</tr>
<tr>
<td>Ischemia/bleeding</td>
<td>17/2</td>
<td>7/2</td>
</tr>
<tr>
<td>Lesion size*</td>
<td>15.4 (7.3)</td>
<td>12.3 (2.3)</td>
</tr>
<tr>
<td>Weeks since lesion</td>
<td>14.1 (23.6)</td>
<td>22.4 (27.7)</td>
</tr>
<tr>
<td>Hand used: R/L</td>
<td>7/12</td>
<td>6/3</td>
</tr>
<tr>
<td>Classification of aphasia</td>
<td>9 global; 3 Broca; 1 Wernicke; 5 amnesic; 1 other</td>
<td>2 global; 0 Broca; 3 Wernicke; 3 amnesic; 1 other</td>
</tr>
<tr>
<td>Token testb</td>
<td>32.5 (26.6)</td>
<td>38.6 (24.0)</td>
</tr>
<tr>
<td>Repetitionb</td>
<td>30.3 (24.7)</td>
<td>43.8 (26.4)</td>
</tr>
<tr>
<td>Written languageb</td>
<td>30.1 (21.9)</td>
<td>40.3 (20.3)</td>
</tr>
<tr>
<td>Namingb</td>
<td>24.8 (21.1)</td>
<td>42.7 (22.6)</td>
</tr>
<tr>
<td>Comprehensionb</td>
<td>34.2 (19.6)</td>
<td>39.7 (22.5)</td>
</tr>
<tr>
<td>Imitation finger postures</td>
<td>14.1 (4.8)</td>
<td>17.4 (2.9)</td>
</tr>
<tr>
<td>Imitation hand postures</td>
<td>15.2 (2.0)</td>
<td>14.8 (4.0)</td>
</tr>
<tr>
<td>Pantomime of tool use</td>
<td>30.1 (10.3)</td>
<td>46.9 (2.5)***</td>
</tr>
</tbody>
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Note: Values in parentheses are SDs.

*Percentage of left hemisphere volume.

bSubtests of AAT, results expressed in percentile of aphasic sample.

***p < 0.001.

Figure 2. (a) Overlay plot of the subtracted superimposed lesions of subsamples of patients with disturbed pantomime (n = 19) minus a group with normal pantomime (n = 9) who were equated for lesion size and language comprehension. (b) Overlay plot of the subtracted superimposed lesions of subsamples of patients with disturbed pantomime (n = 6) minus a group with normal pantomime (n = 5) who all showed normal imitation. The percentage of overlapping lesions of the patients with disturbed pantomime after subtraction of the group with normal pantomime is illustrated by different colors coding increasing frequencies as described in Figure 1. Talairach coordinates (Talairach and Tournoux 1988) of the transverse sections are given. Ins, insula; Pu, putamen; PrCG, precentral gyrus; PoCG, postcentral gyrus; and Wh.mat., white matter.
specifying the type of grip and the directions and sequences of manual actions. It would be tempting to ascribe the deficiency of pantomime following lesions in this location to a loss of this vocabulary. However, as such a vocabulary develops primarily for enabling actual use of tools and objects, its destruction should affect actual tool use at least as much as miming. In contrast, many patients with defective pantomime improve dramatically when allowed to manipulate the tools (Liepmann 1908; De Renzi et al. 1982; Goldenberg and Hagmann 1998; Goldenberg et al. 2004). Apparently, pantomime requires cognitive and neural functions that are not needed for actual tool use.

Both actual use and pantomime are based on knowledge about objects and their function. In actual tool use, this prior knowledge influences selection of motor programs that control the interactions between manual movements and object’s properties. For example, when grasping a glass, scaling of grip width to the width of the glass is achieved by first opening the hand in proportion to, but wider than, the visually perceived width of the glass and then closing it around the glass. Opening and closing are precisely synchronized with the transport movement of the whole hand (Jaennarod 1988), and the strength of the final grip is finely adapted to surface friction and estimated weight of the glass (Johansson and Westling 1984). In pantomime, knowledge about objects and their functions is transformed into motor actions that demonstrate the distinctive features of the object and its use. Thus, when miming to grasp a glass, normal subjects open their hand to the approximate width of the pretended glass at the start of the transport movement and stop the transport at its pretended location without further changing the aperture of their grasp (Goodale et al. 1994; Laimgruber et al. 2005). The width of the aperture demonstrates the width of the glass, and stopping the transport of the hand suffices for indicating the grasp. Pantomime neglects features of object use that are important for manipulation but have little value for discriminating the object, whereas it specifies features that in actual use are determined by the manipulated object. For example, consider the case of ironing: the distance of the hand to the table is determined by the height of the iron, but when ironing is mimed, a distance must be chosen without external support. If this distance falls outside the usual range of iron heights, the pantomime will become unrecognizable. The need to demonstrate features of the action that are hardly attended to in actual use makes pantomime a nonroutine task even when tested for tools that are frequently used in daily living. A further difficulty for selection of appropriate manual actions is posed by the restriction to manual actions which also occur in actual tool use. For example, it is not permitted to indicate the size and shape of the iron by drawing its outline in the air before demonstrating the manner of use.

We propose that IFG injury disturbs the selection of distinctive features of the object and its use, leading to impaired pantomime. Functional imaging studies have consistently shown activation of the left IFG in tasks demanding active retrieval of information from semantic memory as, for example, generation of words belonging to a particular semantic category (Cabeza and Nyberg 2000; Thompson-Schill 2003; Cappa and Perani 2006). With increasing demands on selection between competing alternatives, IFG activity in normal subjects increases and performance of patients with IFG lesions deteriorates (Thompson-Schill et al. 1998; Kan et al. 2006). Pantomime of tool use can be conceived as one instance of active retrieval from semantic memory. From the repository of knowledge about objects and their functions, those features have to be selected that permit recognition of both the object and the manner it is used and that can be demonstrated by manual actions, which are also part of its actual use. On this view, the vulnerability of pantomime to lesions of the left IFG is due to the high demands on selection of a very restrained range of features out of many closely related features that may come to mind when imagining the actual use of the tool.

Our companion study on localization of lesions interfering with imitation revealed that defective imitation of finger postures was associated with lesions similar to those we found responsible for defective pantomime, namely, the IFG as well as the insula and underlying subcortical extension into the putamen and caudate nucleus (Goldenber and Karnath 2006). Interestingly, the fMRI studies that did not find IFG activation by pantomime (see above) both used sequences of single finger movements as the control condition (Moll et al. 2000; Choi et al. 2001). Possibly the similarity of IFG activation by finger movements and by pantomime obscured the contribution of IFG to pantomime. In the present analysis, we found that imitation of finger postures was worse in patients with defective pantomime than in those with intact pantomime, whereas there was no such difference with respect to imitation of hand postures (see Tables 1 and 2). The importance of lesions to left IFG, insula, and precentral gyrus for defective pantomime remained obvious when we analyzed only patients who had imitated both hand and finger postures normally. Nonetheless, the closely related lesion sites responsible for defective pantomime than in those with intact pantomime, whereas there was no such difference with respect to imitation of hand postures (see Tables 1 and 2). The importance of lesions to left IFG, insula, and precentral gyrus for defective pantomime remained obvious when we analyzed only patients who had imitated both hand and finger postures normally. Nonetheless, the closely related lesion sites responsible for defective pantomime than in those with intact pantomime, whereas there was no such difference with respect to imitation of hand postures (see Tables 1 and 2). 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Taken together, the findings of the present and the companion study indicate that pantomime of tool use, imitation of hand postures, and imitation of finger postures rely on different neural and cognitive mechanisms. Traditionally, their disturbances are subsumed under the common label of "ideomotor apraxia," and sum scores from various combinations of these different tasks are proposed for the clinical examination of apraxia (Heilman et al. 1982; Kertesz and Ferro 1984; Alexander et al. 1992; Buxbaum et al. 2005). Our findings add to the growing evidence that such combinations prohibit insights into the specific neural and cognitive mechanisms underlying competency for different domains of manual actions (De Renzi et al. 1982; Barbieri and De Renzi 1988; Rumiati et al. 2005; Della Sala et al. 2006).

Supplementary Material
Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

Notes
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References


