Neural Correlates of Pantomiming Familiar and Unfamiliar Tools: Action Semantics Versus Mechanical Problem Solving?

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Abstract: This study aims to reveal the neural correlates of planning and executing tool use pantomimes and explores the brain's response to pantomiming the use of unfamiliar tools. Sixteen right-handed volunteers planned and executed pantomimes of equally graspable familiar and unfamiliar tools while undergoing fMRI. During the planning of these pantomimes, we found bilateral temporo-occipital and predominantly left hemispheric frontal and parietal activation. The execution of the pantomimes produced additional activation in frontal and sensorimotor regions. In the left posterior parietal region both familiar and unfamiliar tool pantomimes elicit peak activity in the anterior portion of the lateral bank of the intra-parietal sulcus—A region associated with the representation of action goals. The cerebral activation during these pantomimes is remarkably similar for familiar and unfamiliar tools, and direct comparisons revealed only few differences. First, the left cuneus is significantly active during the planning of pantomimes of unfamiliar tools, reflecting increased visual processing of the novel objects. Second, executing (but not planning) familiar tool pantomimes showed significant activation on the convex portion of the inferior parietal lobule, a region believed to serve as a repository for skilled object-related gestures. Given the striking similarity in brain activation while pantomiming familiar and unfamiliar tools, we argue that normal subjects use both action semantics and function from structure inferences simultaneously and interactively to give rise to flexible object-to-goal directed behavior. *Hum Brain Mapp* 32:905–918, 2011. © 2010 Wiley-Liss, Inc.

Key words: gesture; pantomime; apraxia; transitive; tool use; fMRI; action semantics

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INTRODUCTION

Pantomiming the use of familiar tools on verbal or visual command is a way of exploring the integrity of an individual's action repertoire and a central test in the assessment of apraxia [Bartolo et al., 2008; van Heugten et al., 1999]. Despite its clinical relevance, only a limited number of neuroimaging studies have investigated the neural correlates of pantomiming object-related (transitive) gestures [Choi et al., 2001; Hermsdorfer et al., 2007; Imazu et al., 2007; Johnson-Frey et al., 2005; Moll et al., 2000; Rumiaty et al., 2004]. These studies reported predominant

activation in the posterior parietal and prefrontal/premotor regions of the left hemisphere, corroborating the predominant lesion sites of neuropsychological reports on apraxic patients with inaccurate pantomiming [Buxbaum, 2001; Buxbaum et al., 2005a; Haaland et al., 2000]. All neuroimaging studies used highly familiar tools and required the participants to pantomime the normal use of the instrument. However, in daily life tools may also be used in an unconventional way, for example by using the back of a fork to stir your coffee when no spoon is available, or by using a heavy pipe wrench for hitting a nail when you have no hammer. The use of objects to serve a purpose that they were not initially designed for is thought to rely on mechanical or technical problem solving: The ability to understand and make use of the physical properties of objects to achieve a goal. According to Goldenberg and Hagmann [1998], the basis of mechanical problem solving is the ability to infer function from structure and it enables individuals to use unfamiliar tools and to detect alternative uses of familiar tools.

The distinction between mechanical problem solving and action semantics is both clinically and theoretically important. Clinically, several researchers have argued that spared function from structure inference could explain why some patients show (nearly) normal daily use of objects, while they fail to pantomime these same objects on command and show poor conceptual knowledge about the tool, simply because they cannot retrieve the correct information from a damaged semantic memory [Goldenberg and Hagmann, 1998; Hodges et al., 2000]. Theoretically, the concept of mechanical reasoning provides an important alternative to Liepman's original "movement formulae" of stored object-specific movement memories [Liepman, 1920]. Whereas some authors have suggested a facilitating role of mechanical problem solving in object use perhaps triggered or guided by object affordances [Hodges et al., 1999, 2000], others have placed technical reasoning central to object use and have even questioned the role of conceptual knowledge or gesture engrams altogether [Osiurak et al., 2009].

Whatever the importance of the role attributed to mechanical problem solving in object use, all authors seem to agree that this mechanism is fundamentally different from the contribution of conceptual or action knowledge and that it may rely on a different neural network. All the studies on the relation between object use and mechanical problem solving mentioned above are based on neuropsychological experiments analyzing patients' behavioral performance, but provide no neuroimaging data. In this study, we aim to elicit mechanical problem solving by asking normal volunteers to think of and perform gestures with tools that they have never seen before and whose function is unknown to them, and record their brains' hemodynamic response using fMRI. Our paradigm does not offer contextual information and presents the tools in isolation. Gestures based on unfamiliar tools can thus only be inspired by the physical features of the tool that hint its

possible movement and/or purpose. The resulting activation pattern is then compared with the one that is revealed while the volunteers make gestures with familiar tools. Pantomimes of familiar tools are more likely prompted by the recollection of learned object-specific movements. If function from structure inference and action semantics have a different underlying neural substrate and are differently triggered by familiar and unfamiliar tool stimuli, then more qualitatively different patterns of cerebral activation might emerge. On the other hand, correspondence of the activation patterns triggered by familiar and unfamiliar tools would point to a similar approach in the determination of any tool's adequate gestures. The sets of familiar and unfamiliar tools consist of equally graspable objects to control for differences in object affordances [Vingerhoets et al., 2009b] and the participants' performance is recorded and evaluated for compliance and adequacy of the gestures. Inspired by the work of Johnson-Frey et al. [2005], we also make a distinction between planning and executing tool use pantomimes.

MATERIALS AND METHODS

Stimuli

The sets of familiar and unfamiliar tools used in this study were of the same type as those used in an earlier fMRI study on tool knowledge, in which the realization of the tool collection and the rationale for selection were extensively described [Vingerhoets, 2008]. In short, an extended normative group of 135 normal volunteers (92 women and 43 men, Mean (*M*) age 33.1 years, Standard Deviation (*SD*) 17.5 years) rated a collection of 142 common and unusual tools for graspability, knowledge of function, and hands-on experience. On the basis of these ratings, we selected 30 unfamiliar tools that were rated low on functional knowledge and received low experience ratings, yet were considered highly graspable. In fact, functional knowledge ratings of the unfamiliar tools showed that participants had little, if any, understanding of the functional purpose of these tools. A second set of familiar tools was compiled of 30 highly graspable tools that rated high on functional knowledge and received high experience ratings. As a result, while there was no significant difference in the graspability ratings of the two sets, functional knowledge and experience ratings differed significantly, with higher scores for the familiar tools (always $P < .001$). In addition to these two sets, we constructed five different configurations of three similar neutral shapes (graspable and stackable cylinders). A Canon EOS 300D reflex camera mounted on a Photo3D Model 303 adapter (Mission3D, LLC, Exeter, USA) was used to capture a left-eye and right-eye image (stereo pair) of each tool and shape configuration. The aim of the three-dimensional presentation of the target objects through stereoscopic goggles was to enhance the ecological validity of the task. Picture-editing software (Adobe Photoshop and Photo3D mixer)

was used to merge and focus the left and right-eye images on a uniform gray background, oriented so as to be compatible with right-hand grip. Some examples of these stimuli are depicted in Figure 1A and a list of the familiar tools can be found in the Appendix.

Participants

Eighteen healthy volunteers participated in the study. Two volunteers revealed head movements larger than 1 mm on both functional runs and were excluded for further analyses, leaving 16 participants (range: 19–24 years, mean age: 21, 8 women and 8 men). All were right-handed as determined by the Edinburgh Handedness Inventory: $M = 95.4\%$, $SD = 6.3\%$ [Oldfield, 1971]. None had a history of neurological or psychiatric disease. Scanning protocols were approved by the local ethics committee and all subjects gave written informed consent after the experimental procedure had been explained to them.

Procedure

Prior to scanning, the volunteers completed a prescan MRI-safety questionnaire and the Edinburgh Handedness Inventory. They were instructed that they were going to see familiar and unfamiliar tools and that they had to pantomime the correct movements (in case of a familiar tool) or the most likely movements (in case of an unfamiliar tool) with their right (dominant) hand. When performing this task with an unfamiliar tool, they were required to perform the most plausible grasp in order to use the object and make the most plausible movements with it. All unfamiliar tools were highly graspable and had an obvious functional part and a clear handle or grip part, leaving little doubt as to the functional grasp of the tool. The volunteers were allowed to inspect each tool and think of the pantomime they were going to perform for 4,000 ms. During this inspection, a small red cross was projected over the tool. After 4,000 ms, the red cross turned green, signaling the start of the motor response. Pantomiming was then allowed for 4,000 ms until a blank screen with a little red cross was shown for 1,500 ms during which the volunteer resumed the starting position (i.e., right arm resting on the table alongside the body). Participants were also instructed that they were going to see configurations of three identical simple shapes and had to pantomime grasping these shapes and placing them one on top of the other. Here too, a small red cross signaled mental preparation for the movement (4,000 ms), a green cross announced the performance of the pantomime (4,000 ms), and a blank screen with a red cross notified that the starting position had to be resumed. Timing of the protocol and some examples of the stimuli are depicted in Figure 1A. The aim of the study was not explained until the scanning was completed.

The volunteers were positioned head first and supine in the magnet. The left and right arms were placed alongside

the body on the scanner table. A nylon ribbon was tightened over the chest and arms at the elbows, thus limiting movements of the upper arm. Participants were reminded of the fact that MR-imaging is very sensitive to movement and were instructed to restrict head movements and to lie as still as possible to prevent motion artifacts. The procedure also required the subjects to perform the pantomimes rather calmly, using only their right underarm, wrist, and hand. Their heads were gently fixed in place with foam cushions. Stimuli were presented through goggles with an MRI-compatible presentation system that provided a three-dimensional presentation of the stimuli (VisuaStim-Digital, Resonance Technology Inc., California). The virtual screen provided by the goggles measured 76.2 cm at 1.2 m distance resulting in a visual angle of 35° . The visual angle subtended by the stimuli projected on this screen measured 30° .

Stimulus presentation and response recording was controlled by a commercially available experiment generator (Presentation, Neurobehavioral Systems Inc., Albany, CA). The paradigm was arranged as a conventional block design with three conditions. Each condition comprised 10 blocks containing stimuli of familiar tools, unfamiliar tools, or neutral shapes. Each block consisted of the three trials that are described above (mental preparation for 4,000 ms, pantomime performance for 4,000 ms, resuming starting position for 1,500 ms) and thus lasted 28.5 s in total. Every block was separated from the next by an interval of 24 s during which a blank screen was shown. During this interval, the participant was instructed to relax. These intervals were not used in the further analysis but allowed cerebral activation to return to a resting state before the beginning of the next block and limited distortions of the magnetic field due to arm movements from one block to the next [Bandettini and Cox, 2000; Culham et al., 2003]. In total, the experiment took 26.25 min, and was divided into two runs of 13.13 min each. Each run consisted of 15 blocks, five of each condition, which were ordered semirandomly to avoid consecutive presentation of two blocks with the same type of stimuli. Stimuli were randomly distributed over their conditions' blocks. Between both runs, volunteers were allowed a short break and the next run was not started without their permission.

The participants' movements were recorded with an MR-compatible camera (MRC-Systems GmbH, Heidelberg, Germany) that was attached to the head coil and displayed on a computer monitor in the MR control room. A second monitor simultaneously showed the stimuli that were presented. Both monitors were placed side by side and the entire procedure was recorded on mini DV tape by a Canon XM2 digital video camcorder. All sessions were later rated by four additional volunteers who checked whether (i) pantomimes of familiar tools were correct (on a 5-point Likert scale from -2 very inadequate to $+2$ very adequate) and (ii) pantomimes of unfamiliar tools were plausible (on a 5 point Likert scale from -2 very unlikely to $+2$ very likely). In addition to these

Figure 1.

A: Examples of the different conditions and timeline of a condition's block. **B:** Cerebral activation (α (FDR) < 0.05) during planning (red) and execution (green) of pantomimes based on familiar (left panel) and unfamiliar (right panel) tools compared with control transitive pantomimes (block stacking). Yellow boxes highlight posterior parietal activation. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

ratings, the volunteers checked whether the scanned participants complied with the instructions not to move when the red cross was shown and only to pantomime while the green cross was visible.

In the postscan session, participants completed a post-scan MRI safety questionnaire. They were then presented with pictures of the familiar and unfamiliar tools they had seen during the paradigms and instructed to rate each on a 5-point-scale for graspability, knowledge of its function, and hands-on experience. These data allowed us to compare the volunteers' ratings against those of the normative group originally used to select the tools.

Scanning Procedure

Scanning was performed at 3.0 T on a Siemens Trio MRI scanner (Siemens Medical Systems, Erlangen, Germany) equipped with echo planar imaging (EPI) capabilities using an 8-channel PA head coil for radio frequency transmission and signal reception. After automatic shimming of the magnetic field on each participant, a 3-D high-resolution T1 anatomical image of the whole brain in the sagittal plane was acquired for coregistration with the functional images (3D MPRAGE, 176 slices, slice thickness = 0.9, in-plane resolution = $0.9 \times 0.9 \text{ mm}^2$, TR = 2,530 ms, TE = 2.58). Next, 628 functional EPI images in the axial plane were acquired for the entire paradigm (314 during each run). They had the following parameters: TR = 2.5 s, TE = 33 ms; flip angle = 90° , 33 slices, slice thickness = 2.5 mm, slice gap = 1.25 mm, FOV = 192 mm and matrix = 64×64 , resulting in a resolution of $3 \times 3 \times 2.5 \text{ mm}^3$.

Image Analysis

Data analysis was performed using Brain Voyager QX for preprocessing and statistical inference [Goebel et al., 2006]. The functional data set acquired from each run consisted of 314 image volumes. Functional data were subjected to a standard sequence of preprocessing steps comprising slice scan time correction by means of sinc interpolation, 3-D motion correction by spatial alignment to the first volume also by means of sinc interpolation, and temporal filtering using linear trend removal and high pass filtering for low-frequency drifts of three or fewer cycles. Spatial smoothing with a Gaussian filter (FWHM = 8 mm) was applied for the volume-based analysis. The anatomical data for each subject were resampled to 1-mm resolution, and transformed into Talairach standard space using sinc interpolation. The functional data for each subject were coregistered with the subject's 3-D anatomical dataset and transformed into Talairach space.

From each run of each subject's paradigm, a protocol file representing the onset and duration of each block for the different conditions was derived. Factorial design matrices were defined automatically from the created protocols. The BOLD response in each condition was modeled by convolving these

neural functions with a canonical hemodynamic response function (gamma) to form covariates in a general linear model (GLM). After the GLM had been fitted and the effects of temporal serial correlation allowed for (using AR(1) modeling, see [Bullmore et al., 1996]), group (random effects procedure) *t*-maps were generated to evaluate the effects of pantomiming familiar and unfamiliar tools. The specific contrasts that were performed are detailed in the respective parts of the results section below. Since impaired mechanical reasoning as well as defective tool use are predominantly associated with parietal damage, we will focus on this region, but we started with a whole-brain analysis [Buxbaum et al., 2007; Hodges et al., 1999]. First, we analyzed the data set using a whole-volume voxel-wise approach to reveal the BOLD response in the entire cerebrum under the different conditions. Later, more specific contrasts were performed over an a priori determined region of interest (ROI) in order to increase statistical power. Since our hypothesis pertains to the left intraparietal sulcus (IPS) and inferior parietal lobule (IPL), we focused our analysis on the left posterior parietal region only. This region is strongly associated with specific tool use skills and action semantics [Buxbaum et al., 2002, 2006, 2007; Kellenbach et al., 2003; Vingerhoets et al., 2009a] and damage to this area gives rise to apraxia [Buxbaum et al., 2005b; Haaland et al., 2000]. The a priori defined anatomical ROI was drawn on a group-averaged 3-D anatomical image of the scanned group and the brain atlases of Mai et al. [2008] and Talairach and Tournoux [1988] were used for reference. The ROI encompassed the cerebral matter between Talairach coordinates $x = 0$ and -65 , $y = -18$ and -77 , and $z = 21$ and 75 . The anatomical ROI was converted into a volume-of-interest that was used as a mask in conventional GLM-analyses. For all analyses, we used a threshold of $P < 0.05$ corrected for multiple comparisons using false rate discovery (FDR) correction [Genovese et al., 2002].

RESULTS

Behavioral Data

The ratings on graspability, functional knowledge, and expertise attributed to the tools by the participants following scanning were very similar to those of the normative group. Unfamiliar and familiar tools differed significantly on functional knowledge and expertise (always $P < 0.001$), but revealed no significant difference on graspability ($P = 0.86$).

The video-taped performance of each participant was rated on a five-point Likert scale by four separate volunteers (who did not take part in the fMRI procedure) to judge the adequacy of the familiar tools pantomimes (from -2 very inadequate to $+2$ very adequate) and the likelihood of the unfamiliar tools pantomimes (from -2 very unlikely to $+2$ very likely). The average score was $+1.61$ (SD = 0.98) for pantomiming familiar tools, and $+0.33$ (SD = 0.58) for pantomiming unfamiliar tools. Although there was some variability in the subjects' scores, especially for

TABLE I. Brain activation during the planning and execution phase of pantomiming familiar and unfamiliar tools versus control (the planning and execution of nontool related goal-directed transitive movements)

Brain region	BA	Talairach coordinates			Cluster size	$t_{\max}$
		X	Y	Z		
Planning the pantomime of familiar tools: FamTool _{plan} > Control _{plan}						
Right medial frontal gyrus	6	3	-24	59	794	6.74
Left precentral gyrus	6	-17	-15	60	2,332	5.02
Left inferior frontal gyrus	9	-40	7	30	1,858	5.49
Right inferior frontal gyrus	9	42	7	31	760	4.84
Left middle frontal gyrus	46	-44	35	22	1,210	6.00
Right middle frontal gyrus	46	43	29	19	1,020	4.74
Left medial frontal gyrus	10	-6	54	2	358	5.33
Left inferior frontal gyrus	47	-32	30	-7	1,460	5.08
Right inferior frontal gyrus	45	27	30	-4	841	4.68
Left inferior parietal lobule	40	-43	-37	45	4,274	5.67
Left middle temporal gyrus	19	-38	-58	16	362	4.76
Visual areas					64,692	9.26
Executing the pantomime of familiar tools: FamTool _{exec} > Control _{exec}						
L+ R superior frontal gyrus	6	-5	7	58	9,126	7.15
Left postcentral gyrus	2	-54	-28	45	2,894	5.29
Left inferior frontal gyrus	9	-50	5	29	2,421	7.95
Left superior frontal gyrus	10	-28	59	25	3,221	6.46
Left middle frontal gyrus	46	-44	39	15	3,718	7.55
Left precentral gyrus	44	-54	9	11	5,237	6.95
Left inferior parietal lobule	40	-51	-37	52	2,860	5.29
Left middle temporal gyrus	37	-50	-59	0	538	5.54
Visual areas					60,848	9.97
Planning the pantomime of unfamiliar tools: UnfamTool _{plan} > Control _{plan}						
Left precentral gyrus	6	-30	-18	59	1,753	9.05
Left inferior frontal gyrus	9	-42	2	29	1,382	5.04
Left postcentral gyrus	2	-54	-23	37	2,256	5.61
Left inferior parietal lobule	40	-34	-40	51	795	5.07
Left inferior parietal lobule	40	-41	-29	41	1,446	5.58
Visual areas					81,915	9.23
Executing the pantomime of unfamiliar tools: UnfamTool _{exec} > Control _{exec}						
L + R superior frontal gyrus	6	-4	5	58	9,855	8.38
Right middle frontal gyrus	6	42	2	37	1,894	4.80
Left middle frontal gyrus	9	-57	21	34	5,012	6.99
Left superior frontal gyrus	9	-27	52	31	3,308	5.64
Left middle frontal gyrus	46	-45	37	17	8,496	6.33
Left claustrum		-28	24	1	9,975	7.68
Left postcentral gyrus	2	-59	-25	44	6,426	6.77
Left inferior parietal lobule	40	-36	-41	41	3,312	5.94
Visual areas					98,634	9.01

Talairach coordinates refer to the most significant voxel of the activated region at alpha (FDR) < 0.05.

the unfamiliar tools, no one performed in the unlikely or very unlikely range.

Pantomiming Tool Use Versus Pantomiming Transitive Nontool Gestures

To delineate tool-specific pantomime activation, we investigated the activation pattern associated with the planning and execution of familiar tools compared to that of goal-directed and transitive but nontool related movements

(FamTool_{plan} > Control_{plan} and FamTool_{exec} > Control_{exec}). The active regions are listed in Table I and depicted on the left side of Figure 1B. Compared with nontool gesture planning, the planning of pantomimes of familiar tools predominantly activates ventral and dorsal premotor, prefrontal, and parietal regions of the left hemisphere, as well as bilateral occipital regions. Executing pantomimes of familiar tools versus executing nontool gestures activates a similar but almost unique left-hemispheric fronto-parietal and bilateral temporo-occipital pattern, partially overlapping with the planning phase activation (visual areas, left inferior

frontal gyrus, left middle frontal gyrus), but also showing some unique areas of activation (supplementary motor area [SMA], left precentral gyrus, and the anterior-lateral part of the intraparietal sulcus).

Compared with nontool gesture planning, the planning of pantomimes of unfamiliar tools ($\text{UnfamTool}_{\text{plan}} > \text{Control}_{\text{plan}}$) recruits left premotor and prefrontal regions (although somewhat less robustly than familiar tools), left parietal regions, and a substantial part of the visual temporo-occipital cortex (right side of Fig. 1B). The execution of pantomimes of unfamiliar tools versus the execution of nontool gestures ($\text{UnfamTool}_{\text{exec}} > \text{Control}_{\text{exec}}$) reveals a similar pattern that partially overlaps with the planning phase activation (visual areas, intraparietal sulcus, left inferior frontal gyrus), and partially unique areas (SMA, left superior and middle frontal gyrus).

Note the substantial activation over the left intraparietal sulcus and inferior parietal lobule in these contrasts (yellow boxes in Fig. 1B). Within this region two main foci emerge that, at least for familiar tools, appear linked to the planning and execution phases. The first focus, most prominent during the planning phase of pantomimes of familiar tools, is situated on the anterior portion of the lateral bank of the intraparietal sulcus (centering around voxel $x = -42$, $y = -32$, $z = 42$). The second focus, which appears especially active during the execution of familiar tools' pantomimes, occupies a more lateral and slightly more anterior position (centering around voxel $x = -54$, $y = -28$, $z = 45$) on the border of the inferior parietal lobule (Brodmann area [BA] 40) and the postcentral sulcus (BA 2).

Execution Versus Planning of Tool Use Pantomimes

In addition, we investigated the difference in activation between the planning and execution of tool use pantomimes while controlling for nontool transitive pantomimes. The results are shown in Table II and Figure 2A. Executing the pantomime of a familiar tool's use ($[\text{FamTool}_{\text{exec}} > \text{FamTool}_{\text{plan}}] \cap [\text{Control}_{\text{exec}} > \text{Control}_{\text{plan}}]$) reveals additional activation in bilateral precentral gyri ($L \gg R$), bilateral SMA, bilateral inferior frontal gyri ($R > L$), bilateral posterior parietal lobes ($L > R$), bilateral putamen ($L > R$), and the right middle temporal gyrus. The reverse contrast (planning > execution) shows no significant activation. Executing the pantomimes of unfamiliar tools ($[\text{UnfamTool}_{\text{exec}} > \text{UnfamTool}_{\text{plan}}] \cap [\text{Control}_{\text{exec}} > \text{Control}_{\text{plan}}]$) exhibits a very similar pattern. Again, the reverse contrast (planning > execution) reveals no significant activation.

Pantomiming the Use of Familiar Versus Unfamiliar Tools

Finally, we contrasted the activation during the planning and execution of familiar and unfamiliar tools directly. Whole brain analysis at alpha ($\text{FDR} < 0.05$) reveals that

the planning of pantomimes with unfamiliar tools ($\text{UnfamTool}_{\text{plan}} > \text{FamTool}_{\text{plan}}$) shows significant activation in the left cuneus (BA 17, $x = -6$, $y = -80$, $z = 13$, 12 voxels, $t_{\text{max}} = 7.60$). The reverse contrast displays no significant activation. Similar whole brain contrasts for executing pantomimes uncover no significant activation. As we are particularly interested in differences in activation in the left intraparietal sulcus and inferior parietal lobule, an anatomical ROI was drawn over this region, and contrasts were repeated. In the planning phase, no significant differences in activation patterns were observed between familiar and unfamiliar tools. During the execution phase, the pantomiming of familiar tools elicited significant activation in the left inferior parietal lobule (BA 39/40, $x = -50$, $y = -59$, $z = 37$, 3,303 voxels, $t_{\text{max}} = 5.14$). This activation is depicted in Figure 2B.

DISCUSSION

Behavioral Data

The fMRI participants and the normative group that was used to select the tool sets rated the familiar and unfamiliar tools very similarly on graspability, knowledge of function, and expertise. Most importantly, the graspability of both tool sets was deemed to be as good as equal, whereas knowledge of function and hands-on expertise were assessed differently. The low scores on functional knowledge and expertise suggest that the participants had little, if any, knowledge of the exact functional relevance of the unfamiliar tools, and therefore could only rely on their physical properties to provide clues on the possible gestures. External raters considered the participants' pantomimes of familiar tools quite adequate and the pantomimes of unfamiliar tools from neutral to likely. It is important to bear in mind here that the unfamiliar tools were selected on the basis of virtually absent functional knowledge and expertise, and the positive score of the raters suggested adequate compliance with the task.

Cerebral Activation of Tool Use Pantomimes Compared With Control Gestures

Compared with neutral transitive pantomimes, the pantomiming of visually presented tools elicits additional activation in the dorsolateral prefrontal cortex ($L > R$), ventral premotor cortex ($L > R$), SMA, left inferior parietal lobule, left middle temporal gyrus, and widespread temporo-occipital visual areas. The activation of these predominantly left hemispheric frontal and parietal regions during the pantomiming of familiar tools validates most previous neuroimaging studies of pantomiming tool use [Imazu et al., 2007; Johnson-Frey et al., 2005; Moll et al., 2000; Rumiati et al., 2004] and is in line with the localization of the brain lesions in patients with apraxia [Buxbaum et al., 2005b; Haaland et al., 2000].

TABLE II. Cerebral activation during the execution > planning phase of pantomiming familiar and unfamiliar tools controlled for nontool transitive movements

Brain region	BA	Talairach coordinates			Cluster size	$t_{\max}$
		X	Y	Z		
Executing > planning the pantomime of familiar tools: [FamTool _{exec} > FamTool _{plan}] ∩ [Control _{exec} > Control _{plan}]						
L + R medial frontal gyrus	6	−5	−12	49	12,667	9.93
Left precentral gyrus	4	−33	−22	57	31,601	8.33
Left postcentral gyrus	2/40					
Right precentral gyrus	4	36	−14	58	7,636	7.25
Left inferior frontal gyrus	9	−55	5	30	1,610	5.82
Right inferior frontal gyrus	44/9	54	4	18	4,291	6.21
Left inferior parietal lobule	40	−30	−38	54	9,322	6.89
Left inferior parietal lobule	40	−57	−33	23	2,238	4.50
Right inferior parietal lobule	40	30	−38	54	6,070	6.48
Right inferior parietal lobule	40	50	−27	28	6,504	6.28
Left superior parietal lobule	7	−25	−61	61	3,505	5.73
Right superior parietal lobule	7	9	−69	60	922	4.90
Right middle temporal gyrus	39	52	−57	7	879	5.49
Left cuneus	18	−11	−98	13	1,167	5.65
Right cuneus	18	15	−99	12	463	4.82
Left putamen		−24	−2	6	7,967	6.51
Right putamen		27	0	2	6,043	6.50
Executing > planning the pantomime of unfamiliar tools: [UnfamTool _{exec} > UnfamTool _{plan}] ∩ [Control _{exec} > Control _{plan}]						
L + R medial frontal gyrus	6	−2	−10	54	14,695	9.92
Left precentral gyrus	4	−29	−25	59	31,768	8.63
Left postcentral gyrus	2/40					
Right precentral gyrus	4	30	−13	63	11,405	7.64
Left inferior frontal gyrus	9	−54	7	32	1,899	7.28
Right inferior frontal gyrus	44/9	56	3	18	5,656	6.00
Left inferior parietal lobule	40	−29	−40	52	10,493	6.67
Left inferior parietal lobule	40	−52	−35	24	3,867	5.11
Right inferior parietal lobule	40	32	−37	54	5,623	5.56
Right inferior parietal lobule	40	55	−27	27	6,589	6.30
Left superior parietal lobule	7	−14	−66	61	6,707	5.23
Right superior parietal lobule	7	8	−73	60	2,500	4.97
Right middle temporal gyrus	39	52	−58	6	1,032	4.94
Left cuneus	18	−10	−98	13	2,272	6.58
Right cuneus	18	14	−98	12	1,919	5.30
Left putamen		−25	−6	6	8,669	7.25
Right putamen		23	−4	10	7,544	5.97

Talairach coordinates refer to the most significant voxel of the activated region at alpha (FDR) < 0.05.

Frontal Activation

The left inferior frontal and/or ventral premotor cortex is linked with visuomotor transformations for the control of hand posture while grasping and manipulating objects [Binkofski et al., 1999]. This area receives input from the inferior parietal lobule and is part of the so-called ventro-dorsal stream, which is thought to play a role in object awareness, control of hand posture, and action understanding [Rizzolatti and Matelli, 2003; Rizzolatti et al., 2002]. In humans, damage to this region is associated with ideomotor apraxia (IMA) [Haaland et al., 2000].

The present study also identifies activation in several other frontal regions, which was not consistently found in all previous pantomime studies. The activation in the dor-

solateral prefrontal region (BA 9/46), for example, confirms the findings of Moll et al. who attributed this activation to action shifts involved in the flow of pantomimes, as damage to this region does not lead to apraxia, but to perseverative behavior [Moll et al., 2000]. On the other hand, Choi et al. [2001] did not report any dorsolateral prefrontal activity, but noticed activation in the SMA and a dorsal premotor region in coordinates that are very similar to ours. The SMA is involved in the performance of learned, skilled movements and only appears to be significant in our study during pantomime execution, not planning. Another frontal region activated by our paradigm was the left dorsal premotor cortex that has been associated with the selection and retrieval of stimulus-guided movement [Choi et al., 2001; Grafton et al., 1998]

and imagined grip selection [Johnson et al., 2002]. Our results show that, in line with the preparatory nature of such decisions, this activation is only observed during the planning phase of the pantomimes.

To explain the differences in frontal activation patterns across pantomiming studies, it has been suggested that they are caused by differences in the demands of their respective control tasks [Johnson-Frey, 2004]. These control tasks include oppositional finger movements [Choi et al., 2001], repetition of a sequence of complex movements involving fingers, hand, wrist, and forearm [Moll et al., 2000], and moving the hand in a nonmeaningful fashion [Johnson-Frey et al., 2005]. None of these control gestures are transitive movements, but all require close attention to the motor task. It might be that these relatively demanding control tasks removed some of the frontal foci when subtracting them from pantomiming tool use. In this study, the use of a simple transitive movement (stacking) as a control task appears to be able to reveal the different frontal regions that were reported in pantomiming studies.

Parietal Activation

The region that enjoys the greatest consensus regarding tool use pantomimes is situated in the left inferior parietal lobule. This region is strongly associated with specific tool use skills and action semantics [Kellenbach et al., 2003] and damage to this area gives rise to apraxia [Buxbaum et al., 2005b; Haaland et al., 2000].

In this study, the focus of the inferior parietal activation for familiar tools appears to differ between the planning and execution phase of the gesture (yellow boxes in Fig. 1B). A more medial region of activation is situated on the anterior portion of the lateral bank of the intraparietal sulcus (centering around voxel $x = -42$, $y = -32$, $z = 42$) and is more active during the planning phase of pantomiming familiar tools. This region is believed to be the human homologue of the monkey anterior intraparietal (AIP) area, a region strongly implicated with grasping [Culham et al., 2003; Frey et al., 2005; Tunik et al., 2005, 2007]. This activated region is almost identical to the peak voxel activity described by Binkofski et al. ($x = -45$, $y = -35$, $z = 43$ [in 1998] and $x = -42$, $y = -35$, $z = 41$ [in 2000]) and Frey et al. ($x = -40$, $y = -33$, $z = 43$) that was elicited by right-handed grasping movements of meaningless shapes versus pointing or rest [Binkofski et al., 1998, 2000; Frey et al., 2005].

More recent research has linked the human AIP to the encoding and representation of action goals [Hamilton and Grafton, 2006; Tunik et al., 2005]. In one study that independently manipulated goal and target of imagined movements, virtually the same region ($x = -44$, $y = -32$, $z = 47$) was highly responsive to the functional intention toward the tool, rather than to object category [Vingerhoets et al., 2009a]. The results of the latter study suggested a distinction between tool use and tool object-selective inferior parietal regions. Only functional (use) intentions toward an object elicited activation in the anterior

and middle portions of the lateral bank of the inferior parietal sulcus, which suggested involvement in the higher order control of action. On the other hand, grasping movements aimed at familiar tools only activated the convex portion of the inferior parietal lobule, thus implying an association with motor representations for the use of familiar tools. It was argued that this difference between the use-responsive and the object-responsive regions may pertain to the distinction between mechanical and conceptual types of knowledge [Bartolo et al., 2007] and that the AIP area may be involved in mechanical problem solving due to its association with action goals. Interestingly, in the present study, the AIP region not only survives the contrast with a control transitive pantomime but is also especially active during the planning phase of movement, which again hints at a possible involvement in the encoding of the functional goal of the action, and thus perhaps also in mechanical reasoning.

A second, more lateral parietal region, which centers around $x = -54$, $y = -28$, $z = 45$ and is situated on the border of the left postcentral gyrus and the inferior parietal lobule, is especially active when executing the pantomimes of familiar tools. Unfortunately, information about the possible function of this region is scarce. The cortex in the vicinity of this peak voxel was also found to be responsive during the imagined manipulation of familiar tools rather than neutral shapes ($x = -52$, $y = -33$, $z = 44$ [Vingerhoets et al., 2009a]), and also showed repetition suppression for the goal of grasping movements, that is repeated grasping of the same of two common objects regardless of its location ($x = -52$, $y = -32$, $z = 44$ [Hamilton and Grafton, 2006]). Both studies suggest an association with goal-related movements, but provide only little information as to the specific role of this more lateral area, and unfortunately they do not lead to a better understanding of why the medial and lateral foci respond differently to the planning and execution of familiar tool pantomimes. It may well be that both regions are continuous and share the same functions, as we did not see a similar planning/execution difference for unfamiliar tools and these areas did not survive direct comparison of familiar versus unfamiliar tool contrasts (see below). Further light may be shed on this possible distinction within and around the intraparietal area by means of more natural paradigms that distinguish between the parietal activation in planning versus execution and that perhaps apply more time-sensitive registration methods such as MEG.

Occipital and Temporal Activation

The extensive activation of visual areas which was also reported in other studies can be attributed to the visual presentation of the tool stimuli [Hermsdorfer et al., 2007; Rumiaty et al., 2004]. During the planning and execution of pantomimes, this visual activation overlaps considerably, but when subjects are confronted with unfamiliar tools it is somewhat more distinctive. Significant occipital and inferior temporal (in particular fusiform) activation during the observation of unfamiliar tools has been reported before and is believed to reflect increased visual processing of the features and contours of an apparently meaningful tool in an attempt

Figure 2.

A: Cerebral activation (alpha (FDR) < 0.05) during execution > planning the pantomimes of familiar (yellow) and unfamiliar (red) tools corrected for general transitive pantomimes (block stacking). **B:** Activation in the posterior parietal region during the execution of familiar tools' pantomimes compared with the execution of unfamiliar tools' pantomimes (alpha (FDR) < 0.05). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

to recognize and categorize it [Vingerhoets, 2008]. In a pantomiming task, close visual inspection of the tool object is crucial, especially if it is unfamiliar, as motor affordances are predominantly based on the physical features of the object, rather than on its pre-existing conceptual knowledge [Vingerhoets et al., 2009b].

The left posterior temporal cortex is believed to represent semantic information of manipulable objects and their associated actions and is part of the ventral processing stream [Chao et al., 1999; Johnson-Frey et al., 2005; Kellenbach et al., 2005].

Executing Versus Planning of Tool Use Pantomimes

In agreement with previous findings [Johnson-Frey et al., 2005], we ascertained that the execution > planning of pantomimes elicits additional activation in bilateral primary motor and somatosensory cortex (L > R), the SMA, premotor cortex, inferior parietal lobule, and visual areas (especially cuneus). We also detected bilateral activation in the basal ganglia, compatible with the motor requirements in this condition and we observed bilateral activation in

the superior parietal lobule ($L > R$). In sum, there appears to be a very large overlap between the execution $>$ planning contrasts of the familiar and unfamiliar tool conditions. In fact, we are unable to point at any regions that are uniquely active in one condition but not in the other.

Pantomiming the Use of Familiar Versus Unfamiliar Tools

The gesture engram hypothesis proposed by Liepmann states that apraxia is caused by the loss of (or impaired access to) movement formulas, learned spatio-temporal images of intended actions, and considers the impairment as a deficit in manipulation knowledge about objects [Goldenberg, 2003; Liepmann, 1920]. Goldenberg & Hagmann argued that manipulation knowledge about objects can be based on the retrieval of instructions from memory. Alternatively, they claim that it could be attributed to a direct inference of function from the structural properties of tools with the requirements posed by actions, the direct inference hypothesis [Goldenberg and Hagmann, 1998]. This hypothesis is corroborated by the finding that apraxic patients who show impaired actual tool use invariably have defective mechanical problem solving. A broader technical reasoning hypothesis is proposed by Osiurak et al., which disregards conceptual knowledge in the use of objects, but states that an object's use is guided by reasoning based upon abstract technical principles [Osiurak et al., 2009]. The latter hypothesis hinges on the strong correlation between impairment of the conventional use of objects and impairment on a test designed to assess the ability to use objects in an unusual way to achieve a certain goal. Also, if technical reasoning is allowed, for example by offering the patient both the tool (i.e. a hammer) and its recipient (i.e., a nail), then the performance is greatly improved compared to when the patient is given the tool in isolation [Osiurak et al., 2008].

Arguments that favor or dismiss these hypotheses should be provided by neuropsychological studies, but an investigation of the neural correlates of gestures triggered by familiar and unfamiliar tools might shed light on how neurally different these tasks actually are and what processes might be involved. Several patient studies have illustrated dissociations between mechanical problem solving skills and action semantics on object use [Bartolo et al., 2007; Goldenberg and Hagmann, 1998; Hodges et al., 2000]. Recent research on the learning of novel object-related actions has indeed shown that patients with IMA benefit from the affordance of the gesture compared to non-IMA patients and normal controls, suggesting that IMA patients are strongly reliant on object structure in gesture recognition [Barde et al., 2007]. These studies suggest that the human ability to work with tools and objects is reliant on different neural entities that each contribute to an adequate tool-to-goal related behavior and, when

damaged, may be (partly) compensated by the intact parts of the network.

In this study, we focused on the neural correlates of pantomiming familiar tools (expected to trigger action semantics) and pantomiming unfamiliar tools (believed to rely on function from structure inference). Direct comparison of both activation patterns revealed only few differences. Whole brain analysis revealed activation in the left cuneus during the planning of pantomimes for unfamiliar compared to familiar tools. The left cuneus is a region involved with target and novelty detection [Gur et al., 2007], and activation of this region has been reported before during the observation of unfamiliar and rarely used tools [Vingerhoets, 2008]. In agreement with the results of these previous studies, we interpret this activation as a way for humans to process the features of an apparently meaningful, yet unfamiliar tool in order to comply with the task. The fact that this region is only significantly active during the planning and not during the execution phase of pantomimes with unfamiliar tools underlines its involvement with action preparation rather than with action guidance.

ROI-analysis over the left posterior parietal cortex shows no significant differences in activation patterns between familiar and unfamiliar tools during the movement planning phase (no activations survived this contrast), which implies that planning the pantomime of a familiar or unfamiliar tool is based on the same neural network within this left parietal ROI. This seems to suggest that the left parietal network that is responsible for the inference of function from structure (i.e. the cognitive task that presumably underlies the pantomiming of unfamiliar tools) is also engaged when planning pantomimes of familiar tools. This seems to support the technical reasoning hypothesis that questions the role of conceptual knowledge and gesture engrams in object use. However, the same contrast during the execution phase of the pantomimes reveals that familiar tools elicit substantial activation in the lateral convex portion of the inferior parietal lobule. The coordinates of this region are very similar to those reported while familiar tools are observed [Vingerhoets, 2008], the manipulation of familiar tools is imagined [Vingerhoets et al., 2009a], and hand postures for functional object use have to be discriminated [Buxbaum et al., 2006]. This area is also associated with IMA and is believed to store representations of the positions of the limb and hand subserving skilled object related actions [Buxbaum et al., 2003, 2005a]. In addition, learning the use of novel tools in normal volunteers reveals the particular involvement of the left inferior parietal lobule in motor planning for skilled object use [Creem-Regehr et al., 2007]. In short, the left inferior parietal lobule is strongly linked with action semantics and gesture engrams.

The present data suggest that in the left parietal region a pantomiming task based on tool stimuli elicits activation in the intraparietal sulcus and inferior parietal lobule (information derived from the tools $>$ control contrasts). The data further reveal that activation within this region does

not appear to be qualitatively different whether the presented tool is familiar or unfamiliar until the pantomime is carried out. During the execution of the pantomime, only familiar tools trigger activation in the convex portion of the inferior parietal lobule. The question remains why familiar tools do not show activation in this region during the planning of the pantomimes. We suggest that the reason for this is that this region is similarly activated by the unfamiliar tools in the planning phase, and hence does not show in the contrast. When trying to come up with a likely gesture for the unfamiliar tool depicted in Figure 1A, a person may notice that this tool resembles a screwdriver with an angle, and that the hexagonal shape of its functional part is similar to a hex or Allen key, so a screwing motion with the angled handle allowing more forceful screwing might be an option. This example illustrates that in order to determine the probable pantomime of an unfamiliar tool, a person needs both mechanical insight and the retrieval of actions with comparable tools whose associated gestures are familiar. Similarly, it can be argued that the retrieval of the classical pantomime of a familiar tool, for example a hammer, may have to be adjusted depending on its physical or mechanical features, as a reflex hammer and a sledge hammer require a somewhat different approach. Determining the probable pantomime of a familiar tool thus also relies in part on the inference of function from structure. As a result, planning the pantomimes of familiar *and* unfamiliar tool stimuli requires both kinds of information: retrieval of tool-specific gesture engrams and goal-directed mechanical inferences. In the execution phase of familiar tool pantomiming, the operationalization of a tool-specific gesture engram becomes dominant, as is illustrated by the increased activation in the convex part of the inferior parietal lobule in the FamTool_{exec} > UnfamTool_{exec} contrast.

CONCLUSION

In this study, we compared the cerebral activation of healthy volunteers during the pantomiming of familiar and unfamiliar tools. The aim of the latter task was to force the participants to speculate about the possible function of the novel object and to produce the most likely gesture based on mechanical reasoning about its physical features. Compared to transitive nontool gestures, the pantomiming of right-handed tool use elicits activation in a distributed cortical network of bilateral temporo-occipital and predominantly left hemispheric frontal and intraparietal regions. Pantomime execution reveals activation of frontal and sensorimotor regions in addition to the regions that are already activated during the gesture planning phase, a finding that confirms previous research [Johnson-Frey et al., 2005]. A comparison of the planning of pantomimes with familiar versus unfamiliar tools only shows additional activation in the left cuneus in the unfamiliar condition, reflecting increased visual processing of the peculiar object. ROI analysis over the left posterior parietal

cortex to increase statistical power fails to demonstrate differences in the same contrast. As we detected left posterior parietal activation during the pantomiming of familiar and unfamiliar tools compared to control pantomimes earlier, we must conclude that familiar and unfamiliar tools elicit similar responses in this region. Only during pantomime execution do familiar tools show additional activation of a region that is clearly more posterior and lateral compared to the previously described AIP region and is located on the convex part of the inferior parietal lobule. The latter region has repeatedly been described as a repository of skilled object-related actions.

In our opinion, the present data correspond most to the direct inference hypothesis that is proposed by Goldenberg and Hagmann. According to this theory, tool use can be based on either existing semantic knowledge about object specific gestures or on a direct inference of function from structure [Goldenberg and Hagmann, 1998]. The present study furthers our understanding of human tool use, by showing that normal volunteers show almost no differences (left cuneus excepted) in cerebral activation between the planning of pantomimes with familiar versus unfamiliar tools. This implies that the use of any given tool, whether familiar or unfamiliar, could be based on both kinds of information. In daily life, this strategy would allow for the most flexible adaptation of objects to goals. A person may use a rake in the conventional way (i.e. teeth down) to spread a new pile of gravel over a drive way, but once loosely spread, the person may realize that the best way to even out the gravel is by using the rake in an unconventional way (i.e., teeth up, sliding the horizontal ridge of the rake directly over the gravel thus forcing the small stones in a more even surface). This insight is not achieved by accident or following demonstration, but simply by coupling the mechanical properties of actor (a part of the rake) and receiver (the gravel) to achieve a particular goal. This example illustrates that even while using familiar tools in the conventional way, the direct inference mode is not switched off. Similarly, particular features of novel tools may remind us of more familiar tools whose associated gestures can be retrieved from action semantics. Both sources of information are used simultaneously and interactively when planning a tool's pantomime. Only when a conventional pantomime is executed does the region associated with skilled object-specific gestures become dominant, as is revealed by the familiar > unfamiliar tools contrast.

Limitations of Interpretation

A possible drawback of this study is that the concept of mechanical reasoning is limited to simple function from structure inferences rather than by more complex reasoning about object-goal relationships. On the one hand, this may limit the level of mechanical problem solving, but on the other hand it offers better control of stimulus similarity between conditions and it focuses on the mechanical properties of the tools rather than on general problem solving. In addition, the present study does not provide any clues regarding the neural correlates of mechanical reasoning. It

seems likely that the AIP region is involved because of its association with the representation of action goals, but there may also be other regions that contribute to this ability, for example intraparietal or frontal regions. Lesion studies with patients that have difficulties with mechanical reasoning may further our understanding of its underlying cerebral network.

A possible confound is the high similarity between the mechanical and functional grasps of the familiar tools presented, as this would require only limited involvement of action semantics and hence may explain the few differences compared to unfamiliar tools. Although mechanical and functional grasp types of the familiar tools may be similar, several studies have shown that the kinematic properties of a grasp depend on the end-goal of the movement [Ansuini et al., 2006, 2008]. We therefore remain confident that pantomiming an object's functional use requires input from action semantics, and that this information is not available for planning and executing pantomimes with unfamiliar tools.

Another potential confound factor between familiar and unfamiliar pantomimes is the difficulty level. Although we controlled for equal graspability of familiar and unfamiliar tools, thus keeping the difficulty level in grasp affordances between both tool sets similar [Vingerhoets et al., 2009b], it can easily be argued that coming up with a gesture to match a novel tool may be more difficult than to reproduce a familiar gesture from memory. This could lead to stronger or additional activation in the unfamiliar condition and obfuscate any fMRI differences between familiar and unfamiliar pantomimes. As it is impossible to quantify this difficulty level (the external raters' scores merely reflect a subjective and qualitative appreciation that is inappropriate for use as a regressor), a careful interpretation is warranted. On the other hand, we applied the same statistical thresholds throughout the study, and found remarkably little evidence of quantitative differences in activation between conditions. The few qualitative differences that were found have been interpreted in the light of previous research.

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APPENDIX

List of Familiar Tools Used in the Paradigm

Snap-off blade knife, cell phone, coat-hanger, corkscrew (2), ice-cream scoop, house key (3), monkey wrench (3), nutcracker, bottle opener (2), pincers (2), punch (2), sauce ladle, scissors, spoon, stapler (2), garden shears (2), hand brush (2), wire brush, and wire cutters.