INTRODUCTION

Neuropsychological studies have shown that some patients with ideomotor apraxia (IMA), which are mainly due to left parietal lesions, are unable to pantomime the use of tools, despite retaining the ability to manipulate the actual tools in a normal manner (Rapcsak et al., 1995; De Renzi and Lucchelli, 1988). This finding suggests that the neural mechanisms underlying tool manipulation in everyday life differ from those involved with pantomiming tool use.

One explanation for such dissociation between the execution and pantomime of tool use would be the lexical and non-lexical gesture-processing route by Buxbaum et al. (2000). Buxbaum et al. (2000) proposed the neuropsychological model of IMA where the gesture system comprises two types: the dynamic portion of gesture representation, and the stored portion of gesture representation (Figure 1; Buxbaum et al., 2000; Buxbaum, 2001). The dynamic portion of gesture representation reflects procedures and representations involved in on-line coding of body-part positioning over time, and results in an internal dynamic model of body parts with respects to one another (intrinsic egocentric coding), and with external objects in the environment (extrinsic egocentric coding). In contrast, the stored portion reflects a learned, broad representation of gesture (Buxbaum et al., 2000). The intrinsic and extrinsic system is important for processing all gestures, meaningful or not and with or without tools in hand. Thus, the patient’s deficits in intrinsic spatial coding affect tasks that require the relative positioning of body parts in space over time or recognizing the body positioning. However, because the praxis system is interactive, support from stored tool and/or gestured information may augment the deficient body position coding, the patient shows relatively good performance on production, recognition and imitation tasks in which such information is available.

Several studies have indicated relations between motor imagery required for pantomimes and the left inferior parietal lobe (IPL). Parsons et al. (1995) reported that the IPL is involved in analogue mental simulation according to the results of their positron emission tomography (PET) study. In addition, Alivisatos and Petrides (1997) conducted a PET study using mental rotation tasks, finding that significant activation in the left IPL reflected the mental rotation process. Furthermore, the left IPL was activated during the imitation of meaningless finger configurations requiring mental simulation (Tanaka and Inui, 2002). These findings suggest that the IPL is likely to be involved in the explicit retrieval and mental simulation of action components. Thus, we assumed that IPL is the neural basis of the intrinsic system of gesture representation in the IMA model described by Buxbaum et al. (2000).

In order to certify our assumption, and to ascertain the neural basis for the IMA model, we examined the neural processes underlying tool-use behavior, and compared pantomiming and imagining of tool-use using functional magnetic resonance imaging (fMRI). To ensure that activation occurred not simply for hand-object
interactions, but also for tool-use, activation during hand use alone was also measured. By comparing a hand-use task involving interactions between the hand and an object with a tool-use task involving interaction between the hand, a tool and an object, activation related to tool-use itself was determined. We used chopsticks, a familiar tool in Japan, as the tool in the present study. Chopsticks were selected for various reasons. First, the interaction between the tool and object affected by the tool is obvious, and subjects can therefore explicitly imagine how the tool works on the target. Since the present study included an imagining task, use of a tool that was not only familiar to subjects but also simple and easy to imagine using was essential. Second, chopstick use requires a small number of hand and finger movements, and since movement is restricted in the MRI scanner, such a tool was needed to make the task as close as possible to tool-use in daily life. Finally, all subjects in the present study were accustomed to using chopsticks. As one of the aims of this study was to examine the special route for accustomed actions, use of the tool must be well learned and sufficiently difficult to necessitate some kind of specialized model for use in a smooth and accurate manner. Use of a tool with such characteristics enabled investigation of the neural processes underlying actual use and the imagining processes of familiar tools under conditions close to tool-use in everyday life.

**MATERIALS AND METHODS**

**Subjects**

Subjects comprised 12 right-handed subjects (6 women, 6 men; mean age: 26.1 years; range: 18-29 years) with no history of neurological or psychiatric illness. Written informed consent was obtained from all subjects in accordance with the Declaration of Helsinki.

**Task Procedure**

The experiment was conducted while subjects were supine with the head stabilized in a fixed restraint in a 1.5-T Eclipse MRI scanner (Power...
Drive 250; Shimadzu Marconi). A container and chopsticks were placed in a paper tray (30 cm × 13 cm) that was fixed to the abdomen of the subject. A pair of tilted mirrors attached to the coil provided subjects with a view of the hands while maintaining the head in fixed restraint. To prevent subjects from viewing a mirror image, two mirrors were used to project the view of hands and chopsticks.

Using only the right hand, participants performed the following tasks: 1) carefully watching the right hand, which was placed on the starting position, projected by a pair of mirrors (control); 2) executing the action of picking up and putting down pieces of plastic (10 mm × 10 mm × 2 mm) from the tray using chopsticks (TOOL USE); 3) executing the action of picking up and putting down pieces of plastic (10 mm × 10 mm × 2 mm) from the tray using the right hand (HAND USE); 4) pantomiming the action performed in the tool execution task (TOOL MIME); 5) imagining using the chopsticks in the right hand as in the TOOL USE task (TOOL IMAGERY); and 6) imagining using the right hand as in the HAND USE task (HAND IMAGERY). For the TOOL USE and HAND USE tasks, subjects were instructed to manipulate pieces of plastic with chopsticks and with fingers of the dominant right hand as usual. For the HAND IMAGERY, TOOL IMAGERY and TOOL MIME tasks, subjects were instructed to imagine the action, such as holding the tool, moving the fingers and approaching the object to be manipulated, as clear and precisely as possible. The action was repeated throughout the task period. Actions were self-paced except for following auditory directions to initiate and stop the action.

Each subject participated in 4 sessions involving 2 tasks each: Session 1, TOOL USE and HAND USE tasks; Session 2, TOOL USE and TOOL MIME tasks; Session 3, TOOL USE and TOOL IMAGERY tasks; and Session 4, HAND USE and HAND IMAGERY tasks. Each task lasted 24 s and was repeated 4 times/session with a control interval of 16 s between each task. The order of sessions was randomized.

**Magnetic Resonance Imaging**

The MRI scanner was used to obtain blood oxygen level-dependent contrast function images. T2-weighted images were obtained using an echo-planar imaging sequence [repetition time (TR): 4000 msec; echo time (TE): 55 msec; flip angle (FA): 90°; field of view (FOV): 256 mm × 256 mm; matrix size: 64 × 64]. A total of 38 axial slices of 4 mm thickness without gaps were obtained.

**Image Analysis**

The initial 3 scans and final 4 scans were removed to avoid instability. Data analysis was performed using Statistical Parametric Mapping 99 (SPM 99) software (Wellcome Department of Cognitive Neurology, London, UK). Functional images were realigned to adjust for head movement, and realigned images were then transformed into the standard stereotaxic Talairach space using the same MNI template to accommodate inter-subject variability in anatomy. Normalized images were then smoothed using an isotropic Gaussian smoothing kernel of full width at half maximum (FWHM) 8 mm. Low- and high-pass frequency filters were applied to the time series. Hemodynamic response was modeled using a box-car function. First level linear contrasts of parameter estimates for each subject were taken to the second level, and random effect analysis was performed. All activation areas beyond the voxel level threshold of $p < .05$ after correction for multiple comparisons were selected, and those within clusters of $> 5$ voxels were reported from selected areas. Statistical significance of differences between 2 conditions was statistically tested by using paired t-tests ($p < .05$). The 8 comparisons that were statistically tested comprised: i) TOOL USE versus control; ii) HAND USE versus control; iii) TOOL MIME versus control; iv) TOOL USE versus TOOL MIME; v) TOOL IMAGERY versus control; vi) HAND IMAGERY versus control; vii) TOOL USE versus TOOL IMAGERY; and viii) HAND USE versus HAND IMAGERY.

**Results**

Brain areas activated during the execution of tasks are listed in Table I. Compared with control conditions, significant activations ($p < .05$, corrected) occurred in bilateral prefrontal cortices, the left primary motor area, bilateral occipital gyri, bilateral cunei, the left insula, left fusiform gyrus, left cingulate and right lateral cerebellum during TOOL USE. During HAND USE, as compared to the control task, bilateral supplementary motor areas (SMAs) and the left premotor area (PM) and left superior parietal lobule were activated.

When comparing activations during TOOL USE with activations during TOOL IMAGERY, bilateral cerebella and primary motor areas were significantly activated (Figure 2a). Inverse contrast (i.e., TOOL IMAGERY vs. TOOL USE) revealed significant activation of the left IPL (Table II, Figure 2b).

Comparison of TOOL USE and TOOL MIME revealed significant activation in the lateral right cerebellum and bilateral postcentral gyri (Figure 2a). Inverse contrast (i.e., TOOL MIME vs. TOOL USE) indicated significant activation in the left IPL (Table II, Figure 2b).

As the lateral part of the right cerebellum was activated only during TOOL USE and the left IPL was activated during tasks requiring explicit remembering of tool-use behavior, mean signal changes for each task were computed (Figure 3).
Activation in the anterior part of the right cerebellum was increased during TOOL USE, while activation in the left IPL was increased during tasks that required imagining the executed action (TOOL MIME and TOOL IMAGERY).

**DISCUSSION**

Explicit Retrieval and Mental Simulation of Hand Actions and IPL

The left IPL was significantly activated during TOOL IMAGERY and TOOL MIME. This result is consistent with findings of left IPL involvement in tool-use pantomime (Choi et al., 2001; Moll et al., 2000) in addition to the results of mental simulation tasks (Greze and Decety, 2001). Grafton et al. (1997) also reported that silent naming of the use of an object activates the left PM. Taken together, these findings indicate involvement of the left IPL and PM in explicit retrieval of hand-object interactions such as in TOOL IMAGERY and TOOL MIME in the present study, in which subjects were instructed to explicitly imagine tool usage and hand interactions with the tool. The left IPL activation observed in TOOL IMAGERY and TOOL MIME thus appear to be associated with the explicit
retrieval and production of grasping and manipulation of objects. Chao and Martin (2000) reported that the left IPL is involved in the retrieval of information related to the specific grasping of tools. Furthermore, several studies have suggested that the left IPL is involved in the retrieval of hand shapes, particularly for hand shapes associated with objects. Bonda et al. (1995) used mental simulation tasks of the hand and reported that the left IPL is involved in the mental manipulation of body schema of the hand. Buxbaum et al. (2003) reported that IMA patients with left parietal damage displayed deficits in the reproduction of hand-shapes associated with familiar objects. Taking these findings into account, the activation in the left IPL observed in the present study may reflect contributions to retrieval of the tool and planning of manipulation without sensory feedback during TOOL MIME and TOOL IMAGERY.

Compared to this activation of the left IPL in tasks requiring retrieval of the tool and planning of manipulation without sensory feedback, activation...
in the left IPL was not significant in the presence of sensory feedback, during the TOOL USE, even though retrieval and planning of manipulation was required.

**Tool Use Execution**

In contrast, significant activations in bilateral cerebellum and the left primary motor area and primary visual area were observed during TOOL USE when compared with TOOL MIME and TOOL IMAGERY. Conversely, activation in the lateral part of the right cerebellum was not observed during HAND USE, TOOL MIME or TOOL IMAGERY. The activation of the posterior part of the right lateral cerebellum observed only during actual tool-use suggests that different neural networks were involved in actual use of chopsticks compared to imagining use of this well-learned tool. Furthermore, the fact that activation in the lateral right cerebellum was insignificant during HAND USE and TOOL MIME indicates that activation in this area is not simply due to the regulation of right hand movement.

The cerebellum is widely agreed to play an important role not only in motor control of stance and gait, but also in higher cognitive functions such as visual attention, cognitive planning and skilled movement (Grafman et al., 1992). During actual tool use, knowledge of how a tool reacts to given manipulative behaviors represents an essential piece of information. In other words, knowledge of the relationship between the input and output properties of tools is required. Imamizu et al. (2000) reported that the internal model, representing the relationship between input and output properties, for a novel tool is acquired in the cerebellum when usage of the tool is learned, enabling tools to be used naturally, as if they were a part of our own bodies. This model allowed estimation of the motor commands required to accomplish the intended tool-use action without explicitly simulating the plan of intended action. Chopsticks in the present experiment represented a well-learned and familiar tool to all subjects. All subjects were thus likely to have already acquired the internal model for chopsticks, which would be reflected in activation in the lateral part of the right cerebellum during TOOL USE in our experiment.

Peigneux et al. (2004) examined the neural basis of the neuropsychological model for upper limb apraxia as proposed by Rothi et al. (1991). Contrary to our supposition that the activation of the right cerebellum reflects the activation of the internal model for tool-use, Peigneux et al. (2004) concluded cerebellar activity observed during TOOL USE could be explained as contributions to movement regulation and integration of simple movements into more complex ones during actual movement production. However, as mentioned above, the present study compared the brain activities of tasks that required both movement regulation and integration of actions (TOOL USE, TOOL MIME and HAND USE), and a significant increase in activity in the lateral part of the right cerebellum during TOOL USE was observed (Figure 2). This indicates that activity in the right cerebellum during TOOL USE was associated with not only movement regulation, but also the specific cognitive model for tools.

We thus suggest that actual use of a well-learned tool requires involvement of the internal model for a tool in the lateral part of the cerebellum. Actual use must therefore not be treated as equal to pantomime or simple hand-object interactions such as picking up an object by hand and the neural basis underlying not only imitation or pantomime but also actual tool use must be taken into account for understanding of neuropsychological cognitive model of praxis processing.

**IMA Model**

The finding that IPL is involved in TOOL MIME and TOOL IMAGERY, support the IMA model proposed by Buxbaum and colleagues (Buxbaum et al., 2000; Buxbaum, 2001). This model updated the contemporary theoretical model of the praxis system, which incorporates two systems necessary for action production: one containing conceptual information, and the other responsible for spatiomotor processing (Rothi et al., 1991; Roy and Square, 1985). Buxbaum and colleagues’ (Buxbaum et al., 2000; Buxbaum, 2001) model was updated to explain numerous patterns of disorders that the contemporary two-route model could not fully explain. As mentioned earlier, the model outlined by Buxbaum and colleagues (Buxbaum et al., 2000; Buxbaum, 2000) comprises dynamic and stored portions of gesture representation. Here, the intrinsic egocentric coding, which is important for processing gestures, is particularly critical when there is no memorial or extrinsic environmental information to provide support to the spatiomotor procedures, as when gestures are pantomimed since pantomime requires accurate speculation of the dynamic relative position of body parts. As stated, the left IPL, which is involved in retrieval of learned gesture engram for tool use and mental simulation of a hand associated with an objects, was significantly activated during TOOL IMAGERY and TOOL MIME. This activity reflects the process of computation of intrinsic egocentric coding for the appropriate hand motion for tool use. Conversely, in the TOOL USE, due to the extrinsic information such as somatosensory input, the contribution of the left IPL to the retrieval of stored gesture engrams and mental simulation performed by the intrinsic system was thus small relative to that during TOOL MIME and TOOL IMAGERY tasks, as explained by Buxbaum and colleagues’ (Buxbaum et al., 2000; Buxbaum, 2001) model.
The role that right cerebellum plays in the Buxbaum and colleagues’ (Buxbaum et al., 2000; Buxbaum, 2001) model is not clear since their model did not consider the neural basis during real tool-use behavior of normal subjects. Though, one possibility is that the right cerebellum might work as the stored portion of gesture representation explained in the Buxbaum and colleagues’ (Buxbaum et al., 2000; Buxbaum, 2001) model. The internal model of tools in right cerebellum, which are learned and stored, might work to provide augmentative support to the action production when actually using the well-learned tools to reduce the calculation cost of dynamic representation of body required for action production. The validity of our supposition awaits experimental or neuropsychological confirmation.

CONCLUSION

In conclusion, the present study examined the neural basis underlying execution of tool-use and the imagining process. The results provide supporting evidence for the IMA model proposed by Buxbaum (2001), and reveal the selective contribution of the left IPL, which is involved in accessing representational memories, during tasks that require explicit retrieval of information related to tool use. In addition, these findings provide evidence for different neural bases underlying the execution and mental imagery processes, and imply evidence for different neural bases underlying the execution process. When we use a tool that is well learned and familiar, the need for contributions from the left IPL associated with mental imagery is reduced, since the internal model in the right cerebellum required for execution of tool use is involved. Further investigation of the neural processes related to tool-use execution should be undertaken to refine and extend our understanding of the theoretical framework of the praxis system.

Acknowledgements This study was performed through the Advanced and Innovational Research program in Life Sciences from the Ministry of Education, Culture, Sports, Science and Technology, the Japanese Government.

REFERENCES


Toshiro Inui, Yoshida-honmachi, Sakyo-ku, Kyoto city, 606-8501, Japan.

Received 13 August 2004; accepted 11 May 2005