

## Effect of Perceptual Learning on Motor Skills of Hands: A Functional Magnetic Resonance Imaging Study

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Our aim was to clarify the mechanism by which perceptual learning improves motor skills of hands. We included 18 healthy volunteers (age  $21.3 \pm 0.3$  years, mean  $\pm$  standard deviation) in the study with a crossover design. The subjects were randomly classified into 3 groups, and they performed a 2-ball quick rotation task with a hand. The role of perceptual learning in improving the ability to discern the length of a wooden stick held between the left thumb and index finger was studied between the first and second sessions of the task in group A, and between the second and third sessions in groups B and C with a period of rest interval between the first and second sessions. Functional magnetic resonance imaging (fMRI) was performed for each group during the perceptual learning session.

The effect of intervention, in the form of perceptual learning, on the task performance was significantly greater than that of non-intervention in all subjects ( $p = 0.022$ ). Among all the activated brain areas, the bilateral prefrontal cortices, right premotor area, right supplementary motor area, right primary sensory area, right primary motor area, right inferior parietal lobe, right thalamus, and left cerebellar posterior lobe showed positive correlations between the respective contrasts from the single-subject analysis and the behavioral data before and after the interventions ( $p < 0.001$ ). This result indicates a pivotal role of the frontoparietal or frontocerebellar circuits in sensorimotor integration; a specific approach that activates these circuits should be developed for clinical rehabilitation of patients.

Motor skill learning is an important aspect of clinical rehabilitation of patients with motor disabilities caused by various neurological diseases, including cerebrovascular disorder. Motor learning includes both the process in which movement is adapted dynamically and the method by which an order and kind of movements are selected (3, 20). In many cases requiring general rehabilitation, this learning is achieved as a result of repetitive practice of the motion, by which an internal model for motor control in the cerebellum is acquired (11). Imamizu et al. (8) reported that cerebellar activity in the early stages of motor learning is a reaction to feedback error, while that in the second half of motor learning is different.

In clinical rehabilitation involving generalized motor learning, daily exercise is required. A typical example of generalized motor learning is intermanual transfer, where a motor skill learned by one hand is transferred to the other hand. This type of brain function is considered to be associated with the ipsilateral dorsolateral premotor area (10). In addition, the generalization of learning is also employed in producing the movements in different directions from the movement learned in one way (9). Grafton et al. (6) reported that the inferior parietal lobule was involved in the generalization of learning whereby learning acquired with fingers is generalized to the movement of the upper limbs.

In recent years, perceptual learning has been effectively used in the rehabilitation of patients to improve their motor skills without repetitive practicing of the target movement or decrease of pain (4, 12, 14, 15). Perceptual learning is generally thought to enhance the function of the target body part, which may be associated with the generalization of motor learning. However, the mechanism underlying the improvement in motor skills after perceptual learning remains to be clarified. Moreover, the effect of intervention on motor skills varies with each subject. Therefore, a consensus has not been achieved regarding the consequences of perceptual learning on motor skill improvement. In this context, exploring brain activity associated with perceptual learning may serve to clarify the abovementioned mechanisms.

If motor learning by repeated practice leads to the acquisition of an internal model, then an improvement in motor skills can be achieved by perceptual learning using different mechanisms of another internal model. In this study, we used the 2-ball rotation task as an index of finger dexterity (10), and recorded the brain activities before and after perceptual learning by using functional magnetic resonance imaging (fMRI). Our aim was to clarify the mechanism underlying the improvement in motor skills after perceptual learning.

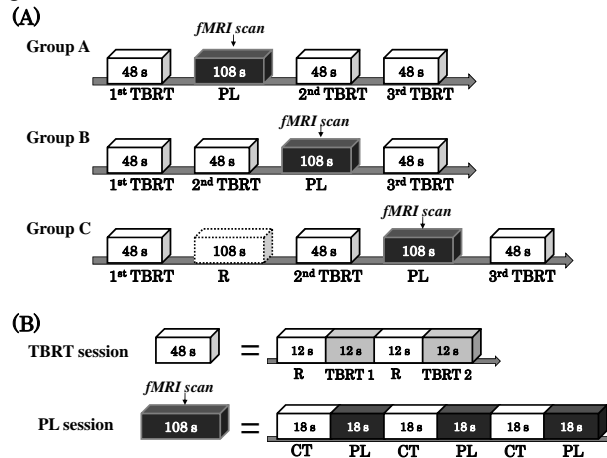
## **MATERIALS AND METHODS**

### **Subjects and general experimental procedure**

Eighteen healthy volunteers (age  $21.3 \pm 0.3$  years, mean  $\pm$  standard deviation) participated in the study. None of the subjects had any signs or histories of medical or neurological diseases, and their brain MRI results were normal. All subjects were classified as strongly right-handed according to the Edinburgh Handedness Inventory (17). Written informed consent was obtained from each subject in accordance with the guidelines approved by the ethical committee of the Kobe University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1975. We employed the crossover design in this study, and the experimental paradigm is illustrated in Figure 1. Participants were randomly classified into 3 groups, A, B, and C. In group A, perceptual learning was achieved between the first and second sessions of 2-ball rotation tasks and between the second and third sessions in groups B and C. During the sessions without perceptual learning, the 2-ball rotation task was performed shortly after the preceding session in groups A and B. In group

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C, the time interval between the first and second sessions was set to be equivalent to the time required for perceptual learning to determine whether the performance of the 2-ball rotation task was affected either by the perceptual learning or by time interval. In this particular time interval, a listening task, which demanded much attention but was unrelated to motor learning, was given so that motor image training was as difficult to perform as in the perceptual learning.



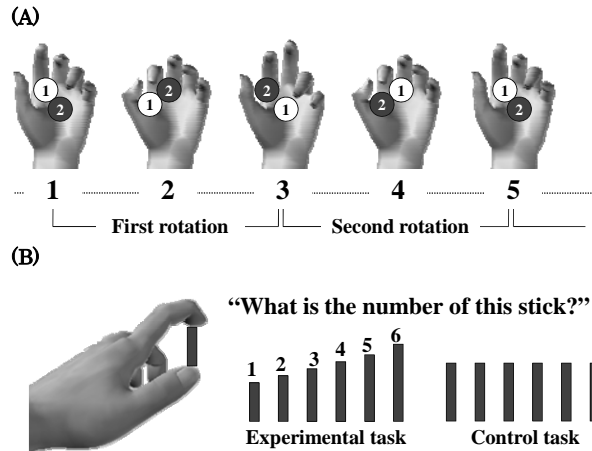
**Figure 1.** Schematic representation of the experimental paradigm. (A) The top of the figure illustrates the experimental sessions of 3 different groups and the time-scale of the associated phases. (B) The bottom of the figure illustrates the time course of the trials both in 2-ball-rotation-task sessions and in perceptual-learning sessions. Functional magnetic regarding imaging (fMRI) scans were performed during the perceptual learning sessions in (A) and (B). TBRT, two-ball-rotation task; PL, perceptual learning; CT, control task; R, rest; and fMRI, functional magnetic resonance imaging.

### Behavioral measurement (2-ball rotation task)

Subjects were placed comfortably in the supine position in the MRI scanner setup in a dark and quiet room, and they performed the 2-ball rotation task with a hand (10). We placed 2 elastic balls, each 3.5 cm in diameter and weighing 20 g, on the left palm of the subjects. The subjects rotated the balls around each other in a counter-clockwise direction using only the left hand, while keeping the right hand at rest. The subjects rotated the balls as quickly as possible for 12 s with their eyes closed. The number of ball rotations was increased by 1 when the positions of the 2 balls were exchanged once (Figure 2A). None of the subjects had ever performed similar motor tasks previously. During the interval period, movement of fingers was not allowed, but the 2 balls were held in the palm. The signal to start or stop the 2-ball-rotation task was an auditory stimulus (a beep tone) provided via a headphone.

### Behavioral data analysis

Skill improvement ratios were calculated from the mean number of ball rotations in each session. We defined the skill improvement ratios between the first and second sessions in group A and between the second and third sessions in groups B and C as the effects of intervention (Figure 1). Further, the change in the ratios of the rotation number between the 2-ball rotation task sessions without the intervening perceptual learning sessions were defined as the effects of non-intervention. Finally, the ratio of the mean effect of intervention divided by the mean effect of non-intervention was defined as the effect index of perceptual learning in each group.



**Figure 2.** One run of the 2-ball rotation task performed using the left hand (A), and representative illustration of the perceptual learning task to improve the ability to discern the length of wooden sticks held between the left thumb and the left index finger (B). A: The participant rotates the 2 balls around each other on the palm in a counter-clockwise direction (phases 1–5). At the end of one rotation, the positions of the balls are exchanged. B: We used 6 wooden sticks of lengths 20, 22, 24, 26, 28, and 30 mm for perceptual learning. For the control task, the participants held a stick of the same length (25 mm) 6 times.

### Perceptual learning task

All visual stimuli were created using Microsoft Office PowerPoint 2003 and projected on a screen positioned outside a scanner approximately 3 m from the gantry. Subjects viewed the projection screen via a mirror mounted on the head coil. During the experiment, the participants were placed in a supine position with the left arm supported by cushions to enhance comfort.

Training to improve the perceptual discernment of the length of wooden sticks held between the left thumb and index fingers was administered in experimental phases (Figure 1B), with the subjects in the supine position in the scanner. A single wooden stick was cut to obtain 6 sticks equal in diameter and 20-, 22-, 24-, 26-, 28-, and 30-mm in length (Figure 2B). The sticks were numbered, and pre-training for the perception of stick length was provided to the participants so that they associated the length of each stick with its number before the commencement of the experiments.

The perceptual learning session consisted of alternating control and experimental blocks (3 of each kind), each block lasting for 18 s (Figure 1B). One block included 6 trials of perceptual learning. In the control trials, the 25-mm long stick was presented for 1 s 6 times, whereas the 6 kinds of different sticks were randomly presented for 1 s each time in the perceptual learning trials. The participants were required to examine the length of the stick held between the left thumb and index fingers and indicate the number of the stick within 2 s. The correct number was then displayed on the screen for 1 s so that the participants could review the correct answer. An fMRI scan was performed for each group during the perceptual learning session (Figure 1A). Participants did not leave the scanner during the experiments.

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### **fMRI data analysis**

An fMRI was performed using a 3.0 T Achieva Quasar dual whole body MRI (Philips, Best, The Netherlands) using an 8-channel synergy-L sensitivity encoding (SENSE) head coil (MRI-Devices, Waukesha WI, USA) and a T2-weighted gradient echo (GE) single-shot echo-planar imaging (EPI) with the following sequence parameters: echo time (TE)/repetition time (TR)/Flip angle = 30 ms/2000 ms/90° and spatial resolution:  $4.83 \times 5.67 \times 3.75 \text{ mm}^3$ . A total of 36 slices were recorded in interleaved ascending mode, which covered the entire brain area (field of view (FOV), 280 mm and rectangular field of view (RFOV), 80%). Several of the initial volumes of each fMRI series were automatically discarded because of non-steady magnetization. We acquired 156 volumes per fMRI session.

The fMRI images were transferred to a personal computer and converted to neuroimaging informatics technology initiative (NIfTI) format using the program MRICroN. Pre-processing of the MRI data was performed with statistical parametric mapping 5 (SPM5) (Wellcome Dept. of Imaging Neuroscience, London, UK) operating under Matlab 7.1 (The Mathworks Inc., Natick, MA, USA). All the functional images were spatially realigned to the first functional image to correct for head motion during the 156 image sessions. The realigned functional images were spatially normalized to the default EPI template in SPM5. After normalization, the data were smoothed using an isotropic Gaussian kernel of 8 mm to improve the signal-to-noise (S/N) ratio. We examined the correlation between the respective contrasts from the single-subject analysis and the behavioral data (the effect index of perceptual learning as a regressor) using SPM5. The correlation was considered significant when the peak-height was beyond the threshold of  $p < 0.001$  uncorrected and the extent threshold of  $k = 30$  voxels. Anatomical localization of the activation peaks was determined from the 3-dimensional (3D) coordinates in Talairach space using the mni2tal tool (MRC Cognition and Brain Sciences Unit, Cambridge, England).

### **Statistical analysis**

We compared the difference between the effect of intervention and the effect of non-intervention on skill improvement in all the subjects using the Wilcoxon test. Differences between the effect index of perceptual learning among the 3 groups were examined using a Kruskal Wallis test. The level of significance was set at  $p < 0.05$ . Statistical analyses were performed using the statistical package for social sciences (SPSS version 12.0 J, Tokyo, Japan).

## **RESULTS**

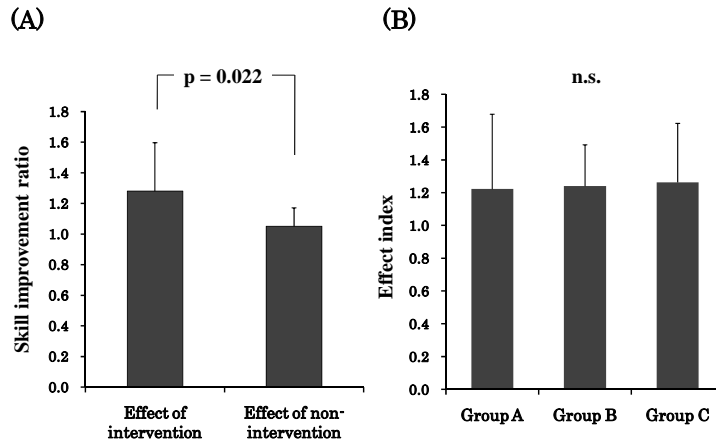
### **Task performance**

The average value of the skill improvement ratio due to the effect of intervention was  $1.28 \pm 0.32$  (range 0.77-2.20) and that due to the effect of non-intervention was  $1.05 \pm 0.12$  (range 0.86-1.33). The effect of intervention was significantly higher than that of non-intervention in group-level analysis ( $p = 0.022$ ), as seen in Figure 3A.

The average value of the effect index of perceptual learning was  $1.24 \pm 0.36$  (range 0.79-2.10). Results of the Kruskal Wallis test indicated no significant differences in the effect index of perceptual learning among the 3 groups ( $p = 0.911$ , Figure 3B). In fact, significant difference was detected between the skill improvement ratio for the effects of intervention and non-intervention in each group.

**fMRI data**

Brain activations related to the perceptual learning are summarized in Table I. During perceptual learning, we observed positive correlations between the respective contrasts from the single-subject analysis and the effect index of perceptual learning in some brain areas, namely the bilateral prefrontal cortices, right premotor area, right supplementary motor area, right primary sensory area, right primary motor area, right inferior parietal lobe, right thalamus, and left cerebellar posterior lobe (Figure 4). We did not observe any negative correlations in this study.



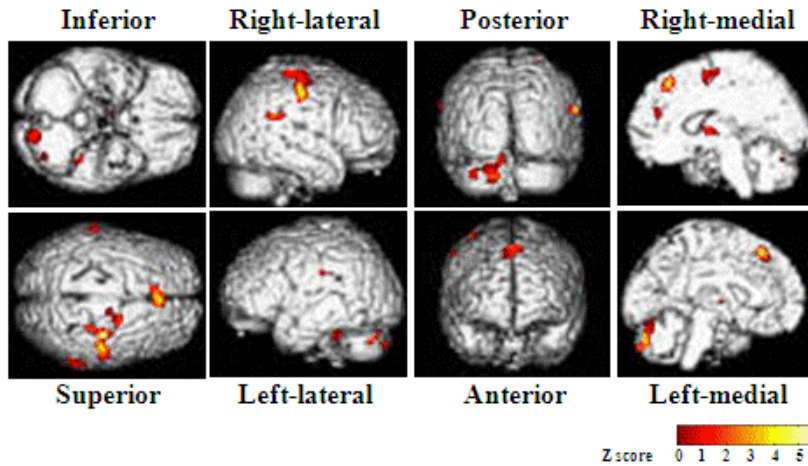
**Figure 3.** Differences between the skill improvement ratio in the groups with the effect of intervention and the effect of non-intervention (A) and differences in the effect index of perceptual learning among the 3 groups (B). A: The effect of intervention on the skill improvement ratio was significantly higher than that of non-intervention. Refer to the Methods section for the effects of intervention or non-intervention on the skill improvement ratio. B: Results from Kruskal Wallis test did not indicate a significant difference between the effect index of perceptual learning among the 3 groups. Refer to the Methods section for the effect index of perceptual learning. n. s., not significant.

**Table I.** Activated brain areas showing positive correlation between the respective contrasts from the single-subject analysis and the behavioral improvement.

Functional regions				Z score	Talairach coordinates		
					x	y	z
R	Cerebrum	prefrontal cortex	BA 9	4.24	8	34	48
L	Cerebrum	prefrontal cortex	BA 9	4.05	-2	30	54
R	Cerebrum	premotor area	BA 6	4.15	24	-6	58
R	Cerebrum	supplementary motor area	BA 6	3.76	14	-14	60
R	Cerebrum	primary sensory area	BA 1,2,3	4.14	46	-22	55
R	Cerebrum	primary motor area	BA 4	3.72	38	-18	66
R	Cerebrum	inferior parietal lobe	BA 40	3.77	59	-45	26
L	Cerebrum	inferior parietal lobe	BA 40	3.53	-65	-24	29
L	Cerebellum	cerebellum posterior lobe		3.97	-16	-78	-34

Talairach coordinates of peak activation with  $p < 0.001$  (uncorrected). R, right hemisphere; L, left hemisphere; and BA, Brodmann's area

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**Figure 4.** Surface projections of color-coded statistical parametric maps (SPMs) superimposed onto stereotactically normalized T1-weighted magnetic resonance images of the standard brain. The colored areas indicate cortical activations associated with the improvement in the effect index during left-hand perceptual learning, and represent threshold of  $p < 0.001$  uncorrected. Prominent activation was observed in the bilateral prefrontal cortices, right premotor area, right supplementary motor area, right primary motor and somatosensory cortices associated with hand functions, right inferior parietal area, and left cerebellar posterior lobe.

### DISCUSSION

The effect of intervention, in the form perceptual learning, was significantly greater than that of non-intervention. Perceptual learning in this study is the ability to correctly discern the lengths of sticks, and this action used in the intervention is completely unrelated to the 2-ball-rotation-task that shows better performance after the intervention. Our results indicate that perceptual learning may improve the dexterity of finger movements, and also suggest the association between perceptual learning and motor skill learning. These results provide useful information for the clinical rehabilitation of patients with movement disorders. The influences of the time interval facilitating motor image training were considered as another mechanism behind the improvement in motor skills. However, since the behavior of subjects in group C was similar to that of subjects in the other groups, the influence of time interval was eliminated.

Our results indicated that the motor skills were improved when motor area and somatosensory area, including bilateral prefrontal cortices, contralateral premotor area, contralateral supplementary motor area, contralateral primary motor area, contralateral inferior parietal lobe, and ipsilateral posterior cerebellum were highly activated during perceptual learning. Kawashima et al. (10) showed that the 2-ball-rotation-task using a single hand enhanced motor learning and showed a positive correlation between the increase in regional cerebral blood flow of the premotor area of both sides and the degree of skill improvement during the 2-ball rotation task training. In the study analyzing the learning process of pointing with arm in the patients with either contralateral or ipsilateral premotor lesions, the premotor area was suggested to contribute to the sensorimotor integration (7). Recently, a study on somatosensory-evoked potentials revealed that the contralateral premotor area and prefrontal cortex play an important role in central sensorimotor integration by influencing the incoming somatosensory input for motor control during continuous contraction of the leg muscle (21). Stoeckel et al. (19) showed bilateral activation of the

premotor and the prefrontal cortex together with the posterior parietal cortex and left superior temporal gyrus during the tactile object discrimination using the right hand. Some studies indicate that the premotor and parietal areas may be involved in sensorimotor information processing (1, 2). Moreover, a few studies suggest that the contralateral supplementary motor area is activated during complex hand movements (10, 13). The premotor area and prefrontal cortex are known to have connections not only to the parietal area but also to the cerebellar posterior lobe, which is reported to be associated with cognitive processing (5, 18). O'Reilly et al. (16) suggested that the nature of perceptual prediction may bias the recruitment of sensory-motor networks in orienting through a region in the posterior cerebellum. In addition, Stoeckel et al. (19) suggested that the prefrontal cortex, particularly, plays a role in the working memory necessary to perform perceptual discrimination. Memorizing a standard length of a stick is required by the brain to be able to correctly distinguish between sticks of different lengths. The length of a stick is judged in relation to a standard length. This kind of a cognitive process may require sensorimotor information from the parietal area and cerebellum. These areas were highly activated in our study, when the effect of perceptual learning was strong, implying that the increased activity of the frontoparietal circuit or frontocerebellar circuit during perceptual learning may contribute to the improvements in subsequent performances of the 2-ball rotation task. Thus, our results may be consistent with the findings that indicate pivotal roles of the prefrontal, premotor, supplementary motor and parietal areas, and the cerebellum in the processing of sensorimotor information; further, these brain areas that are activated are suggested to play some roles in the sensory adjustment for motor control.

This study does not provide direct information regarding the mechanism underlying the perceptual learning-induced improvement in motor skill, and we could not clearly distinguish between the influences of somatic sensations and the cognitive processes owing to the absence of a control group. In addition, we used a small sample size. The abovementioned are limitations of our experimental design, which should be addressed in the future studies.

It is important to note that the effect of perceptual learning on the skill improvement varied among the subjects, and that the effect of intervention is strong only when the frontoparietal and frontocerebellar circuits may be strongly activated. These findings are in contrast to those indicating that perceptual learning is always associated with an improvement in the motor skills. However, rehabilitation programs incorporating the strategy of activating similar frontoparietal or frontocerebellar circuits might help to increase the number of patients who respond positively to such interventions.

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