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A study on brain neuronal activation based on the load in upper limb exercise (STROBE)

Jin-Seung Choi, PhD[a], Mi-Hyun Choi, PhD[a],*

Abstract

This study aimed to determine the level of brain activation in separate regions, including the lobes, cerebellum, and limbic system, depending on the weight of an object during elbow flexion and extension exercise using functional magnetic resonance imaging (fMRI). The study was conducted on ten male undergraduates (22.4 ± 1.2 years). The functional images of the brain were obtained using the 3T MRI. The participants performed upper limb flexion and extension exercise at a constant speed and as the weight of the object for lifting was varied (0 g and 1000 g). The experiment consisted of four blocks that constituted 8 minutes. Each block was designed to comprise a rest phase (1 minute) and a lifting phase (1 minute). The results showed that, in the parietal lobe, the activation was higher for the 0 g-motion condition than for the 1000 g-motion condition; however, in the occipital lobe, cerebellum, sub-lobar, and limbic system, the activation was higher for the 1000 g-motion condition than for the 0 g-motion condition. The brain region for the perception of object weight was identified as the ventral area (occipital, temporal, and frontal lobe), and the activation of the ventral pathway is suggested to have increased as the object came into vision and as its shape, size, and weight were perceived. For holding an object in hand, compared to not holding it, the exercise load was greater for controlling the motion to maintain the posture (arm angle at 90°), controlling the speed to repeat the motion at a constant speed, and producing an accurate posing. Therefore, to maintain such varied conditions, the activation level increased in the regions associated with control and regulation through the motion coordination from vision to arm movements (control of muscles). A characteristic reduced activation was observed in the regions associated with visuo-vestibular interaction and voluntary movement when the exercise involved lifting a 1000-g object compared to the exercise without object lifting.

Abbreviations: fMRI = functional magnetic resonance imaging, SPM = statistical parametric mapping, TE = echo time, TR = repetition time.

Keywords: elbow flexion-extension, fMRI, object existence

1. Introduction

Functional magnetic resonance imaging (fMRI) is used in neuroscience studies on human motion.[1–4] The fMRI has been used in studies on upper and lower limb movements; in particular, the sensorimotor cortex significantly accounts for the upper limb's motor and sensory areas, including the wrist and fingers.[1–4] Regarding brain function, studies have looked into finger movements (finger tapping and finger flexion-extension),[1] variations in grip forces of the thumb and index finger,[2] and wrist and elbow flexion and extension exercises.[3,4] Notably, the brain regions exhibiting neuronal activation for the wrist and elbow movements are identified based on the variation in the flexion and extension degree of motion and repeated frequency.[3,4] However, further studies should be conducted on various motion tasks and types to elucidate the precise mechanism of brain nerve activation regarding human motion.

Although numerous studies have reported on the brain regions activated due to object weight, it is difficult to obtain clear results. Despite inconsistent results, the regions associated with object weight are the dorsal stream,[5] ventral stream,[6,7] frontoparietal regions,[8,9] primary motor cortex,[5] and sensorimotor memory area.[10] In addition, the pathway responsible for perceiving object characteristics such as shape and size is known as the ventral area; however, whether the pathway is also engaged in perceiving object weight has not been determined. Furthermore, no study has yet distinguished between the regions of increased and decreased activation during exercise with object lifting. Therefore, it is necessary to monitor the control mechanisms in the kinetic perspective by analyzing the

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brain responses at the level of neurons during exercise with or without object lifting by identifying the regions of increased or decreased activation during a specific behavior.

Therefore, this study aimed to determine the level of brain activation in separate regions, including the lobes, cerebellum, and limbic system, depending on the weight of an object during elbow flexion and extension exercise using the fMRI. This study also aimed to identify the brain region that perceives the object weight by applying the double subtraction method to extract the specific regions of increased or decreased activation during upper limb exercise with object lifting. The characteristics observed in brain regions depending on the presence of objects during upper limb exercise were also analyzed to provide a valid explanation regarding movement patterns.

2. Methods

2.1. Participants

The study was conducted on ten healthy male undergraduates (22.4 ± 1.2 years) with no history of brain damage. They showed normal cognitive processing and were confirmed as right-handed using the Edinburgh test's revised version. The participants also showed no osteoarthropathy, thereby allowing natural movements. Individuals with claustrophobia or a metallic implant such as a metal pin or a pacemaker that may affect the MRI were excluded. The participants were prohibited from external factors such as smoking, alcohol drinking, and intake of caffeine that may affect brain activation and were given an adequate explanation regarding the study's purpose and contents before the experiment. This study was approved by the Institutional Review Board of Konkuk University (IRB project number: 7001355-202103-HR-426) and complied with the regulations of the Helsinki Declaration. Before the experiment, participants were informed about the study and provided written informed consent.

2.2. Experimental design

Each block of the experiment comprised a rest phase (1 minute) and a lifting phase (1 minute). The experiment was repeated four times, and the total duration was 8 minutes (Fig. 1 [a]). In the lifting phase, the participants were guided to have the back of their right hand upwards to perform the elbow flexion and extension at 90°. The flexion and extension exercise was performed 30 times in 1 minute. Regarding this, two conditions were applied: holding nothing in the right hand (0-g motion) and holding a 1000-g object (1000-g motion). The experiment was randomized; therefore, the participant performed the exercise in one randomly chosen condition, then had a 20-minute rest, and then performed the exercise in the other condition. The inter-trial time (20 minutes) was selected using a preliminary experiment with five participants (23.12 ± 1.6 years) in their 20 seconds. After one trial, the rest time was measured based on possible arm pain and the participant's motor memory and fatigue, and an average time of 18 minutes and 35 seconds was calculated. Therefore, an inter-trial time of 20 minutes was decided as being sufficient for rest. All participants were guided to practice right elbow flexion and extension at 90° before the experiment (Fig. 1 [b]). For the 1000-g object, a plastic ball that would not affect the MRI was used.

2.3. Image acquisition and analysis

The functional images of the brain were obtained using the 3T ISOL Technology FORTE at the KAIST Neuroscience Research Center. Single-shot echo-planar imaging (Repetition time (TR)/Echo time (TE): 3000/35 milliseconds, field of view 240 mm, matrix 64 × 64, slices thickness 4 mm) was used to obtain 35 brain slice images per volume. For the anatomical brain image, a method of T1-weighted image, 3-D FLAIR (TR/TE: 280/14 milliseconds, field of view 240 mm, matrix 256 × 256, slice thickness 4 mm), was used.

The fMRI data were analyzed using statistical parametric mapping (SPM) 12 software (Wellcome Department of Cognitive Neurology, London, UK). All functional images were aligned with the anatomic images of the study using affine transformation routines built into the SPM 12 program. Time series of images acquired from the same participant were realigned using a least-squares approach and a 6-parameter (rigid body) spatial transformation. The first image in the list specified by the user is used as a reference to which all subsequent scans are realigned. The realigned scans were coregistered with the participant's anatomic images obtained during each session and normalized to a template image in SPM 12, which uses the space defined by the Montreal Neurologic Institute. The motion
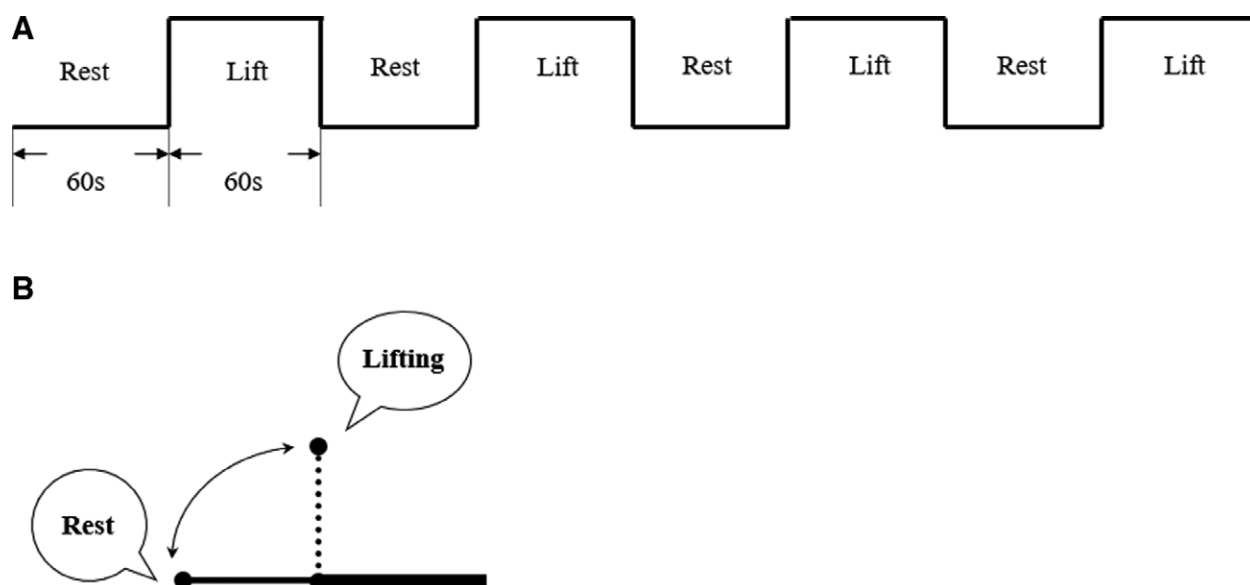

Figure 1. (A) Experimental design and (B) arm movement diagram.

correction was performed using a Sinc interpolation. Time-series data were filtered with a 240-s high-pass filter to remove artifacts due to cardiorespiratory and other cyclical influences. In addition, the coregistered T1 and T2 images were used in a multichannel segmentation routine to extract probabilistic maps of six tissue classes: gray matter, white matter, cerebrospinal fluid, bone, soft tissue, and residual noise. Before the statistical analysis, the functional map was smoothened using an 8-mm isotropic Gaussian kernel. The statistical analysis was performed at the group level using the general linear model and the theory of Gaussian random fields implemented in SPM 12. Group analysis was performed to extend the inference of the individual activation to the general population from which the participants were drawn to list all clusters above the chosen level of significance, as well as the separate (>8 mm apart) maxima within each cluster, with the details of significance thresholds and search volume underneath.

The subtraction method was applied to extract the data of the activated brain regions and activation voxel in the elbow flexion and extension of the lifting phase compared with that for the rest phase for 0-g motion and 1000-g motion (lifting phase–rest phase). The activation voxel numbers for the 0-g motion and 1000-g motion were compared by categorizing the activated regions in the frontal, parietal, temporal, and occipital lobes; cerebellum (declive, tuber, uvula, cerebellar tonsil, and culmen); sub-lobar (thalamus, insula, extra-nuclear, and lentiform nucleus); and limbic system (cingulate gyrus, parahippocampal gyrus, and anterior cingulate). The paired t test was performed to analyze the variation in activation voxels between the two experimental conditions for the aforementioned categorized regions. In addition, the double subtraction method was applied to identify the brain regions with higher activation and lower activation for the 1000-g motion condition compared with that for the 0-g motion condition.

3. Results

Activated areas in the brain were detected by comparing the fMRI data at resting state and under two conditions. The activation voxel numbers were estimated per condition for the frontal, parietal, temporal, and occipital lobes; cerebellum; sub-lobar; and limbic system, and the result is shown in Figure 2. The two conditions varied significantly for the parietal lobe ($P = .037$), occipital lobe ($P = .016$), cerebellum ($P = .011$), sub-lobar ($P = .024$), and limbic system ($P < .001$). In the parietal lobe, the activation was higher for the 0-g motion condition than for the 1000-g motion condition. However, in the occipital lobe, cerebellum, sub-lobar, and limbic system, the activation was higher for the 1000-g motion condition than for the 0-g motion condition.

Table 1 presents the brain regions exhibiting a higher activation level for the 1000-g motion condition than for the 0-g motion condition. The activation was higher in the sub-lobar, including the lingual gyrus, inferior, superior, medial frontal, inferior temporal gyrus, thalamus, the limbic lobe (cingulate gyrus and parahippocampal gyrus), and the cerebellum (declive)
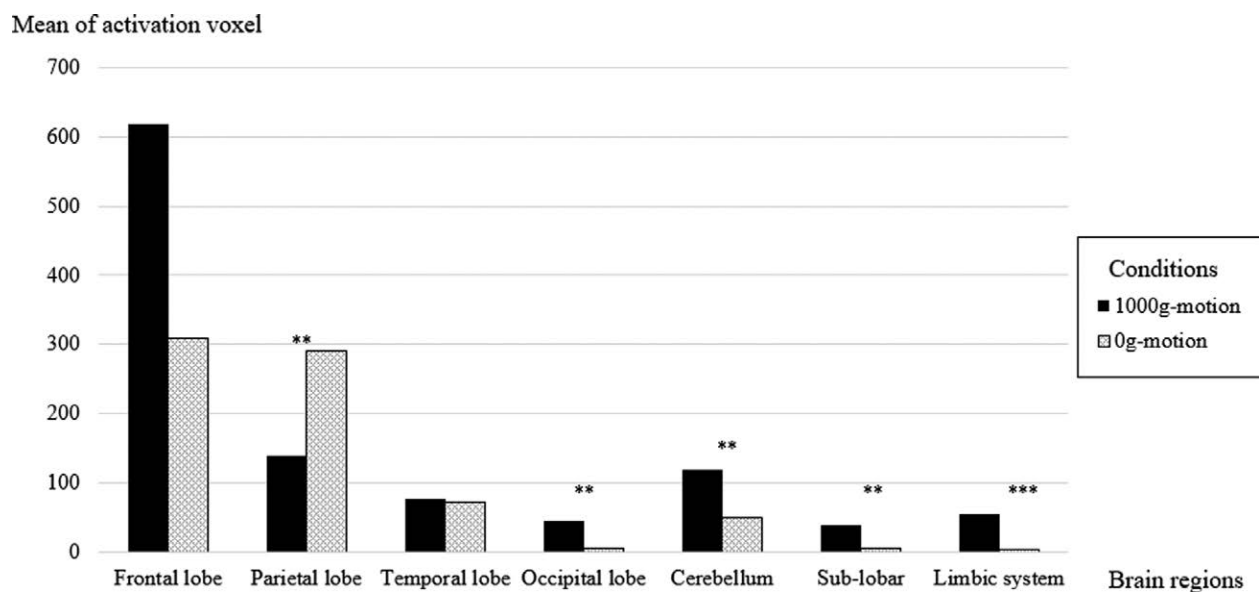

Figure 2. Activated voxel for each area (per condition for the frontal, parietal, temporal, and occipital lobes, cerebellum, sub-lobar, and limbic system).

Table 1

Brain regions exhibiting a higher level of activation for the 1000-g motion condition than that for the 0-g motion condition.

1000-g motion >0-g motion	Area	Peak T value	x	y	z	Activation voxel
Right hemisphere	Lingual gyrus	8.78	3	−78.25	−6	27
	Inferior frontal gyrus	8.13	51.75	19.25	−10	22
	Inferior temporal gyrus	8.58	59.25	−7	−18	21
	Sub-lobar (Thalamus)	7.70	18	−10.75	14	23
	Limbic lobe (Cingulate gyrus)	6.65	3	−40.75	30	27
Right cerebellum	Declive	6.37	21.75	−74.5	−18	18
Left hemisphere	Superior frontal gyrus	8.32	−23.25	34.25	46	21
	Medial frontal gyrus	7.72	−15.75	53	10	36
	Limbic lobe (Parahippocampal gyrus)	8.17	−19.5	−37	−6	16
	Sub-lobar (Thalamus)	7.93	−15.75	−10.75	2	27

(Table 1, Fig. 3). In contrast, the brain regions with a lower activation level for the 1000-g motion condition compared with that for the 0-g motion condition were the superior temporal and parietal region, middle frontal and occipital gyrus, fusiform gyrus, precuneus, and sub-lobar (lentiform nucleus) (Table 2, Fig. 4).

4. Discussion

In this study, the activation voxel numbers of activated brain regions depending on the presence of an object during elbow flexion and extension were compared per lobe, and the brain regions with a higher level of activation and those with a lower level of activation for the 1000-g motion condition than for the 0-g motion condition were identified.

The comparison between the activation voxel numbers for the frontal, parietal, temporal, and occipital lobes, cerebellum, sub-lobar, and the limbic system showed that the activation voxel increased in the 1000-g motion condition than in the 0-g

motion condition for the frontal lobe, the cerebellum, with an influence on the descending motor pathways to produce fine, smooth, and coordinated motion, the sub-lobar, and the limbic system. In contrast, the parietal lobe had increased activation in the 0-g motion condition than that in the 1000-g motion condition.

For the upper limb exercise with an object in hand, it was predicted that the frontal lobe, including the motor cortex region, would be activated to a greater degree due to the object's weight. As predicted, the frontal lobe, including the precentral gyrus, showed a higher activation level when the participant held an object in hand during the upper limb exercise. In addition, the motor cortex is associated with functions such as action planning, motor control, and execution of voluntary movements, and since the participants in this study were requested to repeat the upper limb exercise at a constant speed and angle of 90°, the cerebellum and limbic system as the brain regions associated with motor control and action planning are thought to have been activated.[11] Although it is disputable, in a previous study,
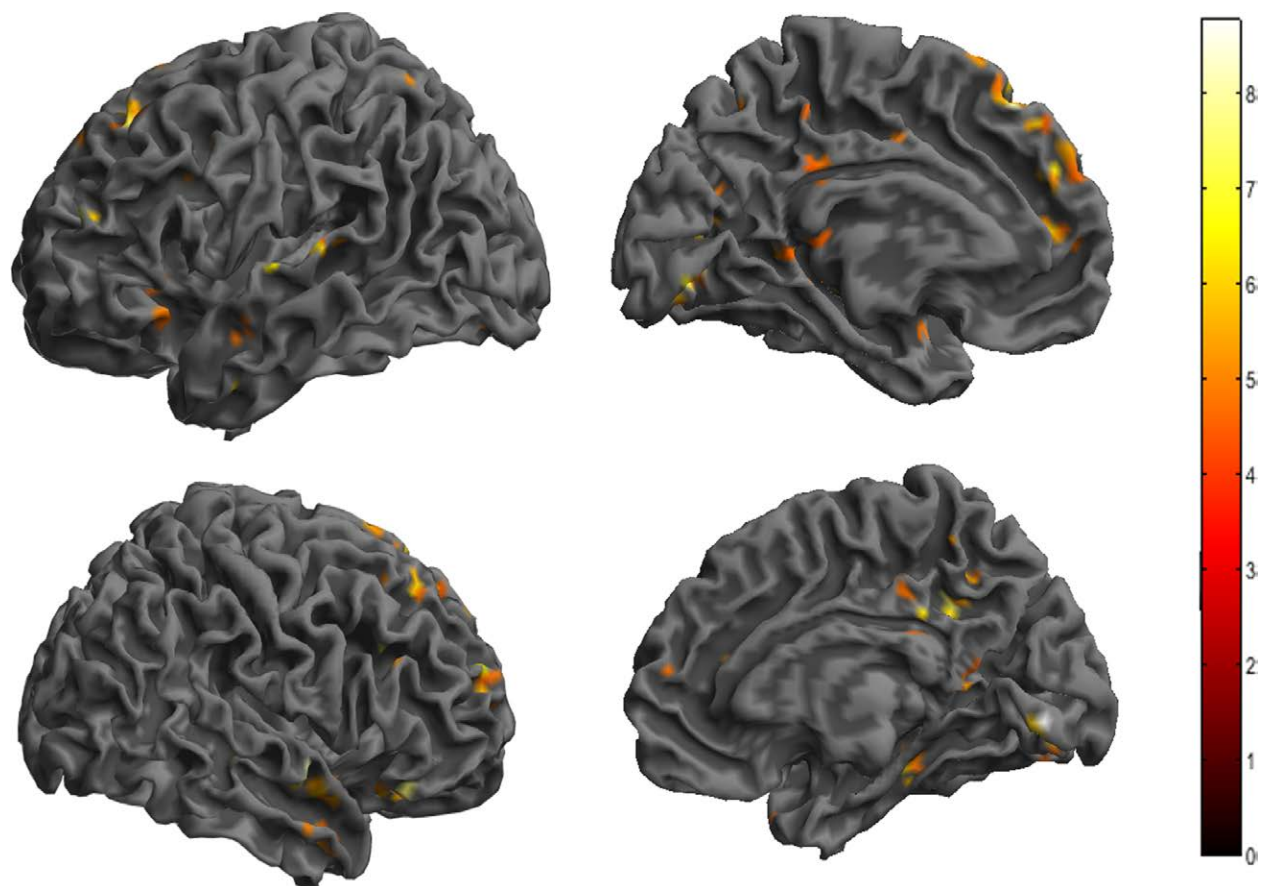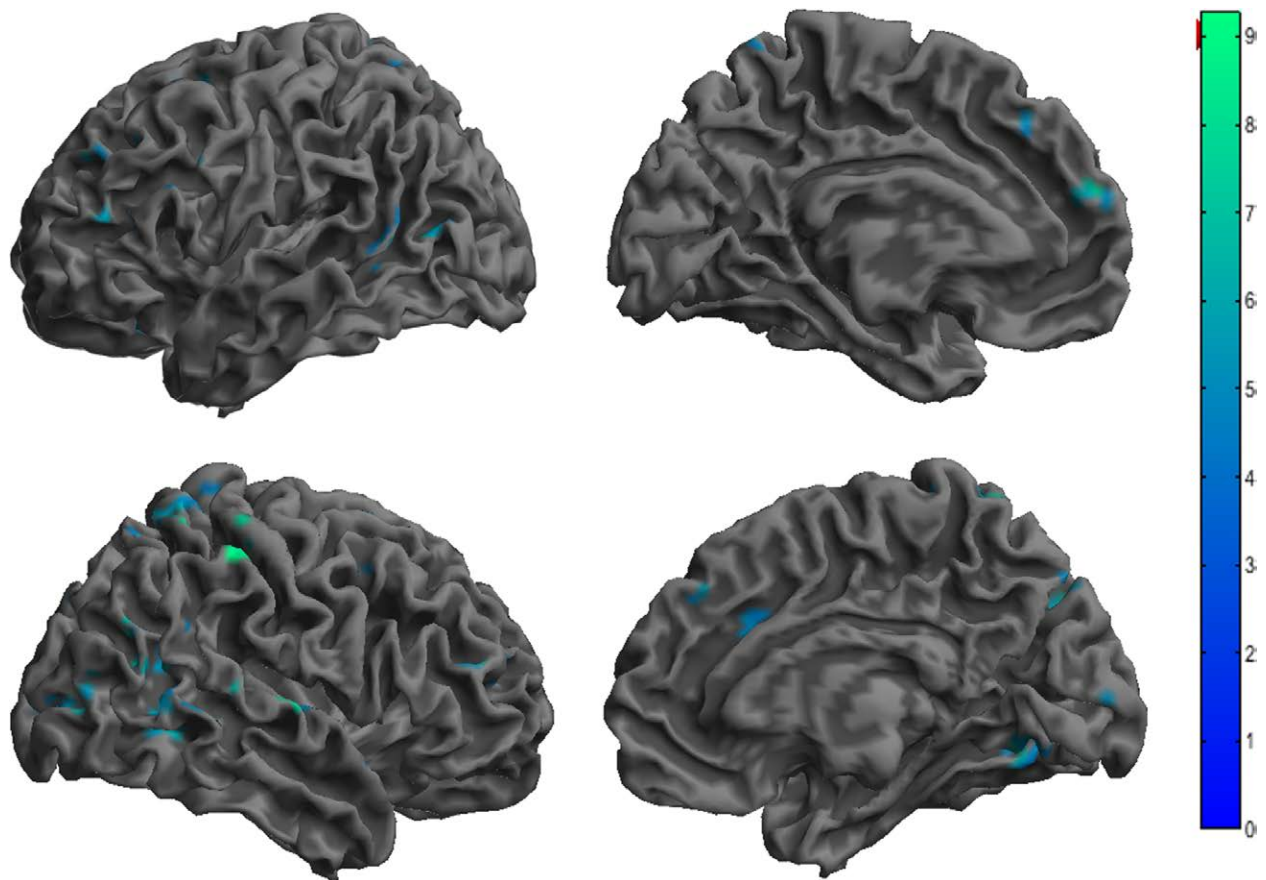

Figure 3. Brain regions exhibiting a higher level of activation for the 1000-g motion condition than that for the 0-g motion condition (corrected $P < .05$).

Table 2

Brain regions exhibiting a lower level of activation for the 1000-g motion condition than that for the 0-g motion condition.

1000-g motion <0-g motion	Area	Peak T value	x	y	z	Activation voxel
Right hemisphere	Superior temporal gyrus	9.50	59.25	−10.75	6	53
	Middle frontal gyrus	8.63	33	0.5	62	12
	Middle occipital gyrus	8.22	33	−85.75	2	27
	Superior parietal lobule	7.92	36.75	−48.25	62	33
	Fusiform gyrus	7.84	21.75	−63.25	−10	19
		6.40	21.75	−78.25	34	15
Left hemisphere	Superior parietal lobule	8.01	−15.75	−55.75	62	9
	Sub-lobar (lentiform nucleus)	6.34	−15.75	4.25	−2	16

Figure 4. Brain regions exhibiting a lower level of activation for the 1000-g motion condition than that for the 0-g motion condition (corrected *P* < .05).

the activation pattern of the primary motor cortex during object lifting was reported to be influenced by the object weight.[6] Moreover, Buckingham et al[7] reported that the activation patterns of ventral stream visual areas were influenced by the correlation between the repeated action of lifting a given object or the surface properties of a given object (color, texture, etc.) and the object weight. The ventral stream visual areas exhibit a pattern of activation based on the perception of shape (lateral occipital cortex) and the surface properties such as texture (posterior fusiform areas near the anterior portion of the collateral sulcus). In Gallivan et al's[6] study, the ventral stream visual area was reported as the region predicting the object weight upon object lifting. Buckingham et al[7] reported that the object weight in patients with bilateral brain lesions was associated with the ventral visual cortex. Fischer et al[9] used fMRI data to conduct machine learning to characterize the brain's expression of object weight (mass). As a result, certain regions of the frontoparietal cortex were shown to be involved in estimating physical variables and predicting the mechanical properties of a given object. In a previous study, the activation of the brain region engaged in the perception of object mass during a perceptual task was observed in the dorsal cortex but not in the ventral areas. Therefore, the suggestion that the frontoparietal cortex and the dorsal or ventral area are "the brain regions associated with object weight" remains controversial.

The ventral area is the region that connects the occipital to the temporal and frontal areas. It is the region associated with action planning[12] and is mainly responsible for the function of "what to stream".[12] It is also the region responsible for object processing and differentiation of color, texture, pictorial detail, shape, and size.[12] The dorsal area is the region that connects the occipital to the parietal area and is associated with the "where and how to stream".[12] The main functions are spatial

processing, movement, and spatial relations.[12] Therefore, interpreting the results in this study based on these two pathways, it is predicted that the ventral area is the region associated with object weight, as the exercise with a 1000-g object increased the activation of the occipital and frontal areas but decreased the activation of the parietal area. Moreover, it is difficult to account for the increased activation of the ventral area solely because the object's weight had been perceived. However, the ventral area and the related regions were found to have been activated to a greater degree than the dorsal area when the exercise was performed with object lifting, through a series of steps from the perception of object weight to the planning and performance of the exercise at 90° and at a constant speed.

Furthermore, the brain regions showing an increase in activation during the exercise with a 1000-g object were identified in this study. The regions with a higher level of activation in the 1000-g motion condition compared with those in the 0-g motion condition were the lingual gyrus, inferior, superior, medial frontal, inferior temporal gyrus, and sub-lobar, including the thalamus, the limbic lobe (cingulate gyrus and parahippocampal gyrus), and the cerebellum (declive). The lingual gyrus is a region corresponding to the occipital lobe, which visually perceives a given object. The inferior temporal gyrus is an important ventral stream region responsible for the object representation's visual processing.[13,14] In addition, the medial superior frontal cortex, including the supplementary and pre-supplementary motor areas, plays an important role in motor and cognitive control.[15–17] The area is also associated with action anticipation.[18] The superior frontal cortex is a sensorimotor-related brain region associated with the motor control network.[19] The inferior frontal cortex is also a part of the ventral stream associated with musical priming and target processing[20] and is thought to be associated with the regions activated at the perception of object

weight and the onset of exercise. Therefore, the activation of the ventral stream, including the occipital, temporal, and frontal lobes that process the data of object identity, was shown to have increased. Furthermore, the comparison of the activation voxel per lobe, as previously described, showed that the activation voxel of the ventral area was greater in the exercise with object lifting. Based on these results, the ventral area is suggested as the region where the perception of object weight occurs. The ventral pathway activation is presumed to have increased as the object came into vision and as its shape, size, and weight were perceived. The results also clearly indicated that visual perception was an important step in the perception of object weight. In addition, activation of the thalamus, a region that mediates the sensorimotor process during the exercise with a 1000-g object in hand and generates the movement with self-monitoring (corollary discharge),[21] was shown to have increased. The regions corresponding to the limbic system also showed a characteristic increase in activation, while the activation of the cingulate gyrus that mediates cognitive processing for behavior regulation and regulates the autonomic motor function[22,23] increased. The cingulate cortex is a region showing many bilateral connections with the cerebral hemisphere's frontal, temporal, and occipital cortices.[24] The parahippocampal gyrus is a cortical region in the medial temporal lobe that surrounds the hippocampus and plays an important role in both spatial memory[25] and navigation.[26] The cerebellum has a fine motor movement function in the control of movement by the frontal lobe. It is presumed to have been activated during the upper limb exercise with object lifting for balance control and motor learning, such as visually guided saccades and motor coordination, including coordination between the eyes and hands and bimanual coordination. The cerebellar decline is a region corresponding to the vermian lobules VI and VII (declive, folium, and tuber), for which a significantly high correlation with cognitive testing was reported.[27] A notable function is its role as the central area controlling saccadic adaptation.[28] For holding an object in hand, compared to not holding it, the exercise load was greater for controlling the motion to maintain the posture (arm angle at 90°), controlling the speed to repeat the motion at a constant speed, and producing an accurate posing. Therefore, to maintain such varied conditions, the activation level increased in the regions associated with control and regulation through the motion coordination from vision to arm movements (control of muscles). Noteworthy is the potential role of a motion navigator to control the motion, simultaneously actively monitoring the motion with the perception of object weight.

Conversely, the regions with decreased activation during the exercise with a 1000-g object compared with those without an object include the middle occipital region and superior parietal lobule in the dorsal stream.[29] The superior parietal lobule is closely associated with the occipital lobe and is involved in aspects of attention and visuospatial perception, including the representation and manipulation of objects.[30–32] Although these regions are critical in the visuo-vestibular interaction function, smooth pursuit, heading perception, optokinetic-related information, the associated optokinetic process,[32] and the activation level during heavy object lifting decreased in this study. Likewise, the activation of the superior temporal cortex with the function of self-motion encoding as a visuo-vestibular-related structure was shown to have decreased.[33] The velocity pathway of the temporal cortical region is a result of the integration of visual (visual motion) and vestibular (body motion) kinetic inputs.[33] In addition, the middle superior temporal area plays a role in processing movement information during ego-motion, and the middle frontal gyrus controls voluntary action upon a task involving the competing response plans or when the behavior of motor sequences is on demand.[34] The precuneus plays a crucial role in executing and attentionally monitoring spatial behavior.[35,36] It is also a region associated with saccadic eye movements, especially the attention to a peripheral visual target.[36] The lentiform nucleus is a region contributing to the coordination of small, precise muscle movements,[37] and damage to this region could lead to a movement disorder. Notably, the regions with decreased activation during the exercise with a 1000-g object compared with those without an object were those associated with the visuo-vestibular interaction and those associated with voluntary movement. Interestingly, the activation of the regions responsible for voluntary movement had decreased. This is presumed to be because, during an exercise with object lifting, the object and the object weight are perceived and because the exercise in this study posed a constraint (the speed of flexion and extension, the flexion angle, etc.) rather than a voluntary movement.

In this study, data regarding kinematics could not be extracted; however, data from neuroscience perspectives may prove valuable in the invasive rehabilitation treatment involving the stimulation of brain regions that are activated during the exercise with an object load for the respective participants with movement disorders. Therefore, a follow-up study will be conducted regarding biomechanics and neurosciences based on kinematics data (movement speed, range, etc.) and kinetics perspectives that can be extracted for upper limb flexion and extension exercise on the electromyography data per mono-articular/bi-articular muscles.

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