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Brain Activity During Predictable and Unpredictable Weight Changes When Lifting Objects

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Schmitz, Christina, Per Jenmalm, H. Henrik Ehrsson, and Hans Forssberg. Brain activity during predictable and unpredictable weight changes when lifting objects. *J Neurophysiol* 93: 1498–1509, 2005. First published September 22, 2004; doi:10.1152/jn.00230.2004. When humans repetitively lift the same object, the fingertip forces are targeted to the weight of the object. The anticipatory programming of the forces depends on sensorimotor memory representations that provide information on the object weight. In the present study, we investigate the neural substrates of these sensorimotor memory systems by recording the neural activity during predictable or unpredictable changes in the weight of an object in a lifting task. An unpredictable change in weight leads to erroneous programming of the fingertip forces. This triggers corrective mechanisms and an update of the sensorimotor memories. In the present fMRI study, healthy right-handed subjects repetitively lifted an object between right index finger and thumb. In the *constant* condition, which served as a control, the weight of the object remained constant (either 230 or 830 g). The weight alternated between 230 and 830 g during the *regular* condition and was irregularly changed between the two weights during the *irregular* condition. When we contrasted regular minus constant and irregular minus constant, we found activations in the right inferior frontal gyrus pars opercularis (area 44), the left parietal operculum and the right supramarginal gyrus. Furthermore, irregular was associated with stronger activation in the right inferior frontal cortex as compared with regular. Taken together, these results suggest that the updating of sensorimotor memory representations and the corrective reactions that occur when we manipulate different objects correspond to changes in synaptic activity in these fronto-parietal circuits.

INTRODUCTION

Adaptation of the fingertip forces to correspond to the physical properties of an object to be lifted involves two control mechanisms called anticipatory parameter control and discrete event, sensory-driven control (Johansson 1996). Anticipatory parameter control is used in advance to specify the appropriate motor commands. It is based on sensorimotor memory representations that store critical properties of the object acquired during previous manipulatory experience (see Fig. 1) (Johansson 1998; Johansson and Cole 1992). The information stored is used to set the parameters of the motor program that generates distributed muscle commands to the muscles producing the fingertip forces. The importance of such sensorimotor memory representations for the retrieval of parameters relevant to motor commands has been demonstrated

regarding the prediction of object's weight (Johansson and Westling 1984, 1988; Westling and Johansson 1987), shape (Jenmalm and Johansson 1997; Jenmalm et al. 2000), and frictional characteristics (Edin et al. 1992; Fagergren et al. 2003; Johansson and Westling 1984). At the same time, the motor system uses an efference copy of the motor command (Von Holst and Mittelstädt 1950) produced when the movement is made to predict the sensory inputs of the motor act (Wolpert et al. 1995) and compares it with the sensory input produced by the movement (Fig. 1).

The discrete event, sensory-driven control policy uses somatosensory mechanisms that sense discrete mechanical events in the digit-object interface and monitor task progress during actual manipulation. Disturbances occurring during task execution—arising from erroneous parameter specification of the motor commands or external disturbances—are reflected by a mismatch between the predicted and the actual sensory input. Such a mismatch triggers reactive prestructured motor patterns specifying the appropriate corrective force responses (Johansson and Westling 1988) together with an update of the sensorimotor memory representations of the object physical properties used in anticipatory parameter control (Fig. 1).

While the neural substrate for several control functions involved in the performance of precision grip-lift tasks in humans have been identified (Ehrsson et al. 2000, 2001, 2003; Kinoshita et al. 2000; Kuhtz-Buschbeck et al. 2001), little is known about the neuronal counterparts of the sensorimotor memory representations of hand-object interactions proposed in the theoretical models of dexterous manipulation. In the present study, we examine two sensorimotor events required in the performance of a precision grip that, according to the theoretical model outlined in the preceding text, should be associated with particularly extensive neural computation. We designed a prototypical lifting task and used functional magnetic resonance imaging (fMRI) to register the blood-oxygenation level-dependent (BOLD) signal as an index of local increases in synaptic activity in the brain (Logothetis et al. 2001). We compared three lifting situations where the possibility of referring to a sensorimotor memory representation to use an anticipatory parameter control to target the object weight varied. When the subjects lifted an object with identical weight in consecutive lifts (*constant* condition), according to the model shown on Fig. 1 (Johansson and Westling 1988), the same sensorimotor representation should be used to program

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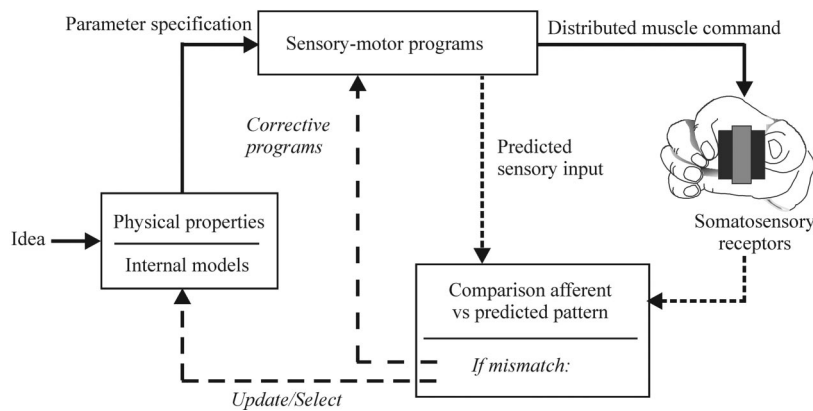


FIG. 1. Adapted from Johansson (1998). Internal models are needed to specify the parameters of the sensorimotor program responsible for the execution of a well-programmed lift. The distributed muscle command targets the grip and the load forces that are to be applied to the object. The somatosensory system predicts the sensory inputs prior to grasping, and as the object is grasped, it compares them to the sensory information provided by the somatosensory receptors. If the predicted and the actual sensory input are identical, the same parameters will be used for the next lift. If, however, there is a mismatch between the predicted and the actual sensory input, the somatosensory system triggers reactive preprogrammed patterns of corrective responses that immediately adjust the forces in the ongoing lift. Concomitantly, the system updates the internal model, which will then be used for the next lift.

the forces applied to the object. When the object weight was changed after each lift regularly between a heavy and a light weight (*regular* condition), because the sequence was known, the subjects were expected to use the serial order strategy (light-heavy-light-. . .) to switch between two sensorimotor memory representations and correctly parameterize in advance the forces to apply to the object. Last, when the weight of the object was changed at random in an unknown sequence (*irregular* condition), we expected the motor command to be targeted erroneously to the previous weight. The mismatch that would result from the comparison of the predicted sensory input and the actual sensory input was expected to trigger an update of the engaged sensorimotor representations.

We hypothesized that the regions activated during regular (predictable) and irregular (unpredictable) weight changes would be part of the cerebral and subcortical network previously shown to be used for precision grip lifts (see Ehrsson et al. 2000, 2001, 2003; Kinoshita et al. 2000). This network includes the primary motor cortex (M1), the bilateral dorsal and ventral premotor cortices, area 44, the supplementary motor area, the cingulate motor area, and several parietal areas in both hemispheres (parietal operculum, supramarginal cortex and intraparietal cortex). In the subcortical areas, the bilateral hemispheres and right vermis of the cerebellum, left basal ganglia and thalamus are also recruited (Kinoshita et al. 2000). Further, we hypothesized that some of these areas would be more active in the regular and irregular conditions because these conditions involved a switch of the sensorimotor object representation and a strong mismatch, respectively, that would result in corrective reactions and an update of the memory representation. Finally, we expected some of these areas to be more active during the irregular condition than during the regular condition because of the larger errors occurring in the programmed fingertip forces during unexpected weight changes.

METHODS

Subjects and general procedure

Twelve right-handed subjects (mean age: 29 ± 3 yr; 7 male, 5 female) participated in the study. All gave their written informed consent, and the study was approved by the Ethical Committee of Karolinska Hospital. During the experiments, the subjects rested comfortably in a supine position in the MR scanner. A plastic bite bar was used to restrict head movements. The extended right arm, used for the experiments was oriented parallel to the trunk. The subjects were

asked to use the tips of the index finger and thumb in a precision grip to lift a test object ~ 5 cm above a support. The lifting movement was produced by a radial flexion of the wrist. We used supports to minimize movements in proximal joints. The subjects were blindfolded, and they wore headphones to reduce the noise from the scanner and to give auditory instructions relating to the task.

Apparatus

The test object, shown in Fig. 2, had a nonmagnetic instrumented handle with vertical flat parallel contact surfaces spaced 30 mm apart (35×35 mm) that were covered with sandpaper (No. 320). The handle was connected by a taut string to a dish located outside the MR-scanner to which an extra weight of 600 g could be easily added and removed between trials by the experimenter. The total weight of the object could have one of two values, 230 (light) or 830 g (heavy). The grip force, perpendicular to the surfaces, and the vertical load force, tangential to the surface, were registered continuously by force transducers in a fiber optics system. The vertical position of the object was measured with a fiber optics transducer.

Lifting task

The subjects lifted the object, following the pace set by an auditory metronome that made a sound of 1-s duration every 2 s (0.5 Hz). Subjects performed three different lifting conditions that differed from each other only with regard to the sequence in which the two weights were presented; a rest condition was also included. In the first condition (constant), the weight of the object was kept the same during consecutive lifts. This condition included either 18 lifts with the heavy weight (constant^{heavy}) or 18 lifts with the light weight (constant^{light}). In the second lifting condition (regular), the heavy and

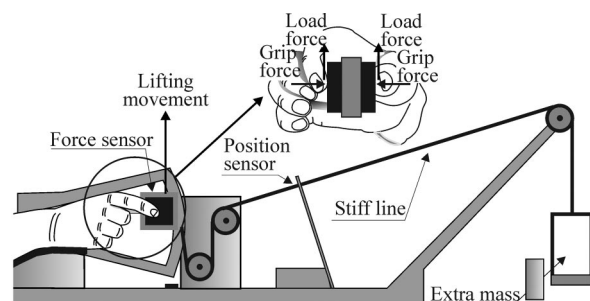


FIG. 2. The precision grip lifting task. A small handle designed to measure the mean grip force and the load force was grasped between the pulps of the index finger and the thumb (see inset). The same posture of the hand was adopted in all conditions. The arm was supported from the shoulder to the radial side of the hand so that the lifting movement occurred at the wrist joint. An extra mass could be added outside the magnetic resonance (MR) scanner between lifts by the experimenter. For details, see METHODS.

light weights were exchanged between every lifts so that the subjects knew the sequence of lifts. During the last lifting condition (irregular), the weight of the object changed unpredictably between heavy and light. In this condition, there were also 18 lifts, and the weight was changed 10 times, i.e., the same weight was used for one to three lifts before it was changed. Figure 3 illustrates 10 lifts from the three different lifting conditions. During the resting condition (baseline; not shown), the subjects relaxed their hand without applying a grip force. The metronome was played through the headphones exactly as it had in the different lifting conditions. Before each condition, a verbal instruction of 4-s duration indicated to the subject the beginning of a new condition. The order of presentation of the different lifting conditions and the resting condition was varied across subjects. Before scanning, subjects were trained to correctly lift the object in

accordance with the instructions during 10 min. They were asked not to apply an excessive grip force.

Behavioral analysis

A flexible data-acquisition and analysis system (SC/ZOOM, Department of Physiology, Umeå University, Umeå, Sweden) was used to sample signals from the force and the position sensors (400 samples/s) time locked with the MR scanner. The grip and load forces were measured and the mean values taken for the thumb and the index finger. Touch was determined by an off-line inspection of the grip force trace and was defined as the moment at which the grip force started to increase. For each lifting trial, the vertical position, the static grip, and load forces were calculated as the value of the force 1 s after touch when the object was held steadily in the air. The peak rate of grip force increase was assessed from the first time derivative of the grip force signal using a ± 5 points numerical differentiation, i.e., the force rate was calculated within a window of ± 12.5 ms. Repeated-measures ANOVAs were used to evaluate the influence of lifting condition (constant, regular, irregular) and object weight (230 and 830 g) on the vertical position, static grip force, and the maximum grip force rate during the load phase. During the irregular condition, the previous weight (230 and 830 g) was analyzed with repeated-measures ANOVA on the same dependent variables. The level of probability selected as statistically significant was $P < 0.05$. The values reported in the figures for data pooled across trials for all subjects refer to means \pm SD.

Brain imaging

Functional MRI was performed on a 1.5 T scanner (Sigma Horizon Echospeed, General Electric Medical Systems) equipped with a head-coil. A high-resolution T1-weighted anatomical image volume of the whole brain (3D-SPGR), and functional gradient-echo, echo-planar (EPI) T2*-weighted echo planar images with BOLD contrast were collected [with settings: field of view (FOV) = 22 cm; matrix size = 64×64 ; pixel size = 3.4×3.4 mm; echo time (TE) = 50 ms; and flip angle = 90° for the BOLD images]. Each functional image volume comprised 30 slices of 5.4-mm thickness that covered the whole brain (including the cerebellum). Two runs were collected per subject. Each run, lasting 608 s [repetition time (TR) = 4 s], included a total of 152 functional volumes. In every run, each of the lifting conditions and the resting condition were performed three times using a block design. Each block lasted 40 s. To allow time for the equilibration of T1, six volumes were recorded and discarded before each run.

Images were processed and analyzed using the Statistical Parametric Mapping software (SPM99; <http://www.fil.ion.ucl.ac.uk/spm/>; Wellcome Department of Cognitive Neurology, London). The functional images were realigned to correct for head movements, coregistered to each individual anatomical T1-weighted image and normalized (transformed by nonlinear transformations) to the standard coordinate system of Talairach and Tournoux (1988) and the Montreal Neurological Institute (MNI) standard space. The functional images were spatially smoothed with an 8-mm full-width at half-maximum (FWHM) isotropic Gaussian filter.

INDIVIDUAL SUBJECT ANALYSIS (LEVEL 1). We applied a general linear model to the functional data, using covariates for the five conditions: constant^{heavy}, constant^{light}, regular, irregular, and rest. We also included the head-movement parameters as regressors in the model to eliminate any activity that might correspond to head movement artifacts. The covariates were convolved using a canonical hemodynamic response function. We used the movement parameters estimated during the realignment preprocessing to model potential movement-related artifacts to eliminate movement-related activity in the data. Parameter estimates and variance were derived for each

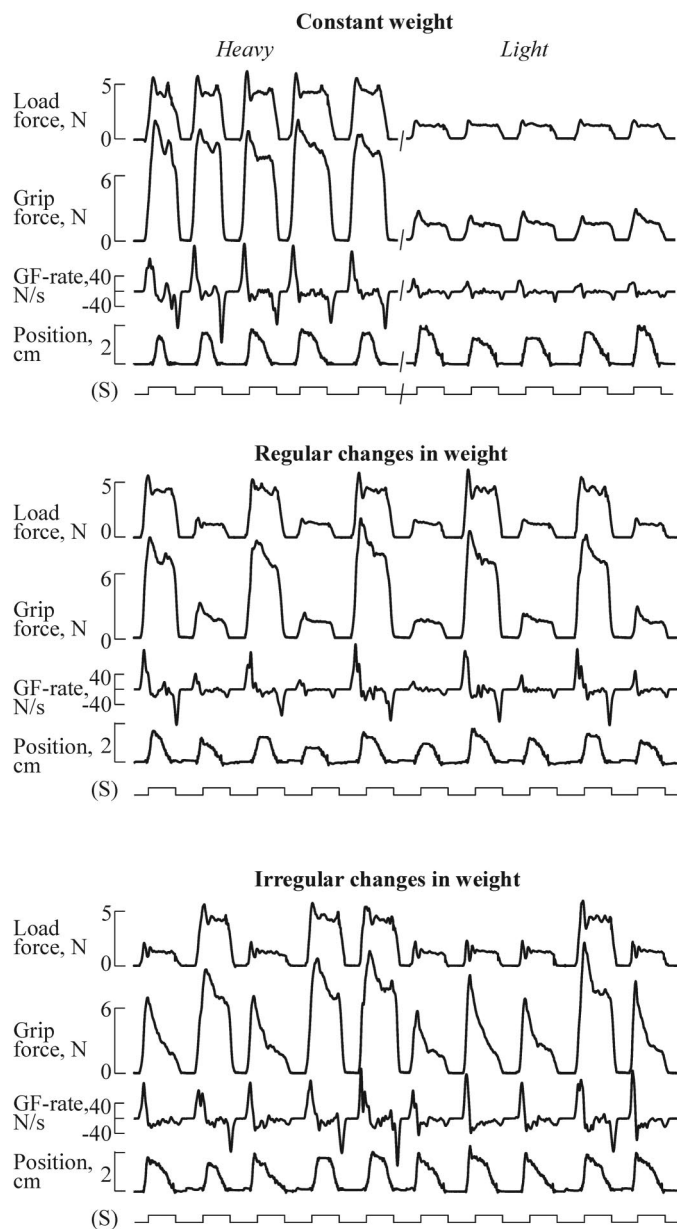


FIG. 3. Representative repetitive lifting trials ($n = 10$) from each lifting condition (constant, regular, irregular). The fingertip forces and the vertical position of the object are shown as a function of time for 10 trials from each condition. Each lifting trial was initiated by a 1-s-long sound (S) at a frequency of 0.5 Hz.

covariate in a subject-specific fixed effects model. We computed the statistical images corresponding to the contrasts: (regular – constant), (irregular – constant), (irregular – regular) and each lifting task minus the resting baseline. Note that when defining these contrasts we “pooled” the data from constant^{heavy} and constant^{light} (constant = constant^{heavy} + constant^{light}). The rationale for this was to match the mean object weight in the constant, regular, and irregular conditions.

RANDOM-EFFECT ANALYSIS (LEVEL 2). To accommodate intersubject variability in group analysis, the contrast images obtained from level 1 were entered into a second level *t*-test, to create an SPM (*t*) map. A one-sample *t*-test was used (11 df). Voxels were identified at $P < 0.05$ after correction for multiple comparisons. We restricted the search space for our analysis to the sensory motor system that is known to be active during precision grip tasks. For the most important contrasts, i.e., (regular – constant), (irregular – constant), and (irregular – regular), we used a region of interest mask that corresponded to the main effect contrast of all lift tasks minus rest (regular – rest + irregular – rest + constant – rest). This contrast is orthogonal to the pair-wise contrasts in the preceding text (i.e., statistically independent) and can thus be used for this purpose. The region-of-interest mask included bilaterally the premotor cortex, inferior frontal gyrus, thalamus, putamen, and cerebellum. In the left hemisphere, the primary sensori-motor cortex, supplementary motor area (SMA) and parietal operculum were included, together with the intraparietal cortex and supramarginal gyrus in the right hemisphere. In addition, we report activations detected anywhere in the brain at $P < 0.001$ uncorrected because the random effect approach is so conservative. Last, a conjunction analysis was conducted to detect those areas that were activated in both the contrasts (regular – constant¹) and (irregular – constant²) ($P = 0.05$ corrected using the region of interest mask defined above). Because we had collected twice as many image volumes during constant as compared with the other two conditions, we could divide these volumes into two identical, but statistically independent, constant conditions, constant¹ and constant², which is required in the conjunction analysis.

Anatomical localizations

The anatomical localization of the activations was determined according to the major sulci and gyri (Duvernoy 1999) distinguishable in a mean standardized anatomical MRI obtained from six subjects. We used the cytoarchitectonic maps in stereotaxic space available on-line (<http://www.bic.mni.mcgill.ca/cytoarchitectonics/>) that were produced by a collaboration between the Medical Institute of the Research Centre Juelich and the Montreal Neurological Institute to relate our inferior frontal activation to the cytoarchitectonically defined area 44 (Amunts et al. 1999). For the cerebellum, we used the terminology of the Schmahmann Atlas (Schmahmann et al. 2000).

RESULTS

Fingertip forces

The performance of the different lifting conditions was consistent across subjects. There was no effect of condition on the vertical position of the lifted object ($P > 0.05$). All subjects used a stronger static grip force for the heavy weight in all three lifting conditions ($P < 0.001$, Fig. 4A; see also Fig. 3). The static grip force for the light weight was slightly higher during the irregular condition than it was for the constant and the regular conditions ($P < 0.001$).

The earliest time at which somatosensory information on object weight can be obtained is after lift-off. Thus the occurrence of the peak grip force rate prior to lift-off is a measure of the parameter setting of the motor program generating the force

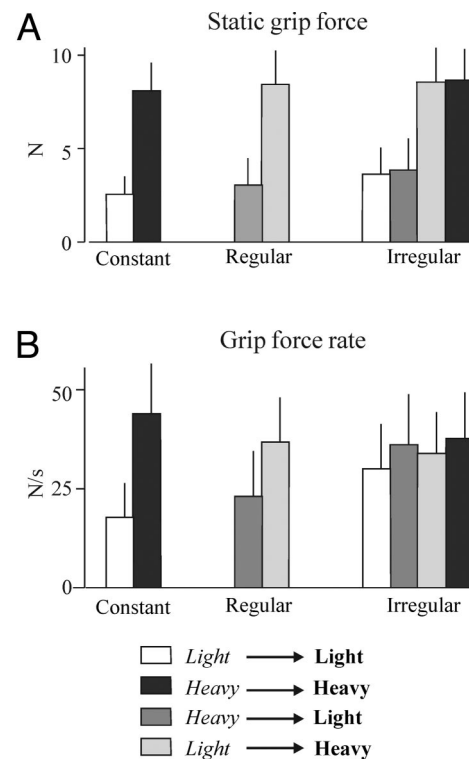


FIG. 4. Static grip force (A) and maximum grip force rate during the phase of isometric grip force increase (B) in the constant, regular, and irregular conditions for both the current weight (heavy and light) and previous weight (heavy and light). The weight of the previous lift is indicated in italics, the weight of the lift used for measurements is indicated in bold. Vertical bars give the means ± 1 SD.

output. During the lifting condition when a constant weight was used, the peak grip force rate was clearly targeted for the light or heavy weight, as applicable, with significantly different amplitudes being observed (Fig. 4B; $P < 0.001$). During the regular condition, the peak grip force rate was also influenced by the object weight, i.e., it was larger for the heavy weight ($P < 0.001$). However, the difference between the peak grip force rate for the light and heavy weights was smaller than during the constant condition (Fig. 4B; see also Fig. 3), indicating less confidence in the precision of the force to apply and a resultant need for small corrections. During the irregular condition, there was no difference in the peak of the grip force rate between light and heavy weight (Fig. 4B, $P > 0.05$; see also Fig. 3). Subjects could not predict the weight changes and, as a consequence, the grip force output was usually targeted close to the value appropriate for the heavy weight. In this condition, we also studied whether there were any effects that could be attributed to anticipatory parameter control in this condition, i.e., if the weight of the previously lifted object influenced the grip force rate (see Gordon et al. 1993; Johansson and Westling 1988). When the previous weight was heavy, the grip force rate was larger than when the previous weight was light, regardless of whether the present weight was heavy or light (Fig. 4B, $P < 0.001$). Thus in this condition, the internal representations were updated after each lift and the anticipatory parameter control influenced the grip force rate in subsequent lifts. In addition, the force output was updated after lift-off (see Fig. 4A).

TABLE 1. *Lifting tasks versus baseline (main effect)*

Anatomical Region	Talairach Coordinates			Peak z score	Cluster Size ³	P value
	x	y	z			
Constant weight versus baseline						
Left central sulcus (S1/M1)	-36	-24	51	5.96	882	<0.001 ¹
Left gyrus precentralis (PMD)	-33	-15	57	5.32		0.009 ¹
Cingulate sulcus (CMA)	-3	-9	45	5.64		0.003 ¹
Medial superior frontal gyrus (SMA)	-3	-6	60	5.25	923	0.012 ¹
Medial cerebellum (Lobule V/VI)	3	-66	-12	5.51		<0.001 ¹
Right lateral cerebellum (Lobule V)	15	-57	-21	5.44		0.006 ¹
Right lateral cerebellum (Lobule V/VI)	24	-51	-27	5.37	80	0.008 ¹
Right lateral cerebellum (Lobule VI)	36	-57	-30	5.30		0.010 ¹
Left lateral cerebellum (Lobule VI)	-30	-57	-27	4.39		0.007 ¹
Left lateral fissure	-51	3	-3	4.33	63	0.020 ¹
Left parietal operculum	-51	-24	12	4.10	33	0.039 ¹
Right lateral fissure	51	3	-6	3.48	21	<0.001 ²
Right supramarginal gyrus	66	-33	21	3.70	10	<0.001 ²
Left ventral thalamus	-15	-21	0	3.35	4	<0.001 ²
Regular changes versus baseline						
Left central sulcus (S1/M1)	-36	-24	51	5.91	983	<0.001 ¹
Left gyrus precentralis (PMD)	-33	-12	54	5.00		0.033 ¹
Cingulate sulcus (CMA)	-3	-6	42	5.76		0.002 ¹
Medial superior frontal gyrus (SMA)	-3	-6	57	4.99	835	0.035 ¹
Cingulate sulcus (SMA/CMA)	-6	6	45	4.98		0.036 ¹
Right lateral cerebellum (Lobule V/VI)	24	-51	-27	5.37		<0.001 ¹
Right lateral cerebellum (Lobule IV/Crus I)	36	-54	-30	5.10	107	0.029 ¹
Medial cerebellum (Lobule IV)	6	-51	-9	4.92		0.044 ¹
Left lateral cerebellum (Lobule VI)	-27	-60	-27	4.55		0.001 ¹
Right inferior frontal gyrus/pars operculum (BA44)	57	12	0	4.27	48	0.043 ¹
Left parietal operculum	-54	-24	15	4.07	82	0.005 ¹
Left lateral fissure	-48	3	0	4.06	54	0.031 ¹
Left ventral thalamus	-15	-21	3	3.67	41	0.020 ¹
Right supramarginal gyrus	69	-33	18	3.52	13	<0.001 ²
Left inferior precentral sulcus (Area 44/area 6)	-60	9	12	3.66	5	<0.001 ²
Irregular versus baseline						
Left central sulcus (S1/M1)	-36	-24	57	5.59	473	<0.001 ¹
Left postcentral gyrus (S1)	-36	-33	54	5.29		0.011 ¹
Medial superior frontal gyrus (SMA)	-6	-6	57	4.88	266	<0.001 ¹
Right lateral cerebellum (Lobule V)	12	-54	-21	5.19	686	<0.001 ¹
Right lateral cerebellum (Lobule V/Lobule VI)	24	-51	-27	5.06		0.027 ¹
Left lateral cerebellum (Lobule VI/Crus I)	-33	-63	-30	4.96	89	0.003 ¹
Right inferior frontal gyrus/pars opercularis (BA44)	57	12	0	4.27	51	0.036 ¹
Left parietal operculum	-66	-24	18	4.11	67	0.013 ¹
Right supramarginal gyrus	66	-33	21	3.86	29	0.043 ¹
Left lateral fissure	-51	3	0	3.69	28	0.046 ¹
Left ventral thalamus	-9	-18	6	3.46	29	0.043 ¹

¹ Corrected *P* values using a small volume correction. ² *P* < 0.001, uncorrected. ³ Number of cubic 27 mm³ voxels in cluster.

Brain activation: all lifting conditions minus rest

The brain regions showing stronger activity when the subjects performed the three lift conditions as compared with the resting condition are shown in Table 1 and Fig. 5. All conditions were associated with a significant increase in activity in the contralateral M1 and primary somatosensory cortex (S1), the SMA, the cingulate sulcus (CMA), and the bilateral cerebellum, (*P* < 0.05 corrected; Fig. 5, A–C, Table 1). Peaks of activation were observed in the left parietal operculum in the constant and regular conditions, and in the irregular condition, a cluster of active voxels extended into this area. Furthermore, peaks of activation were observed in the right inferior frontal gyrus in the regular and the irregular conditions, and in the constant condition, a cluster of active voxel also extended into this area (*P* < 0.001 uncorrected). We related the location of the inferior frontal activation to the cytoarchitectonic maps of this area in MNI space published on <http://www.bic.mni.mcgill.ca/cytoarchitectonics/>. Our peak of activation was located at a

voxel in standard space where 30–40% of the brains have area 44 located. Thus it is likely that the activation in the right inferior frontal gyrus corresponds to area 44. We also observed peaks of activation in the left lateral fissure (at *P* < 0.001 uncorrected for the constant condition) in all lifting conditions. The clusters of active voxels extended superiorly to the inferior frontal gyrus pars opercularis. Using the results of the single-subject analysis superimposed on the individual anatomical pictures, we found that in eight of the subjects, the activity was located around the left lateral fissure and extended both into the inferior frontal gyrus and in the superior temporal gyrus. In three subjects, the activity was found in the superior temporal gyrus only, and in one subject, the activity was found in the inferior frontal gyrus only. Significant activations (at *P* < 0.05 corrected or *P* < 0.001 uncorrected) were also observed in the right supramarginal gyrus and the left ventral thalamus in all three lifting conditions. In the primary sensorimotor area, a large cluster of active voxels extended into the precentral gyrus

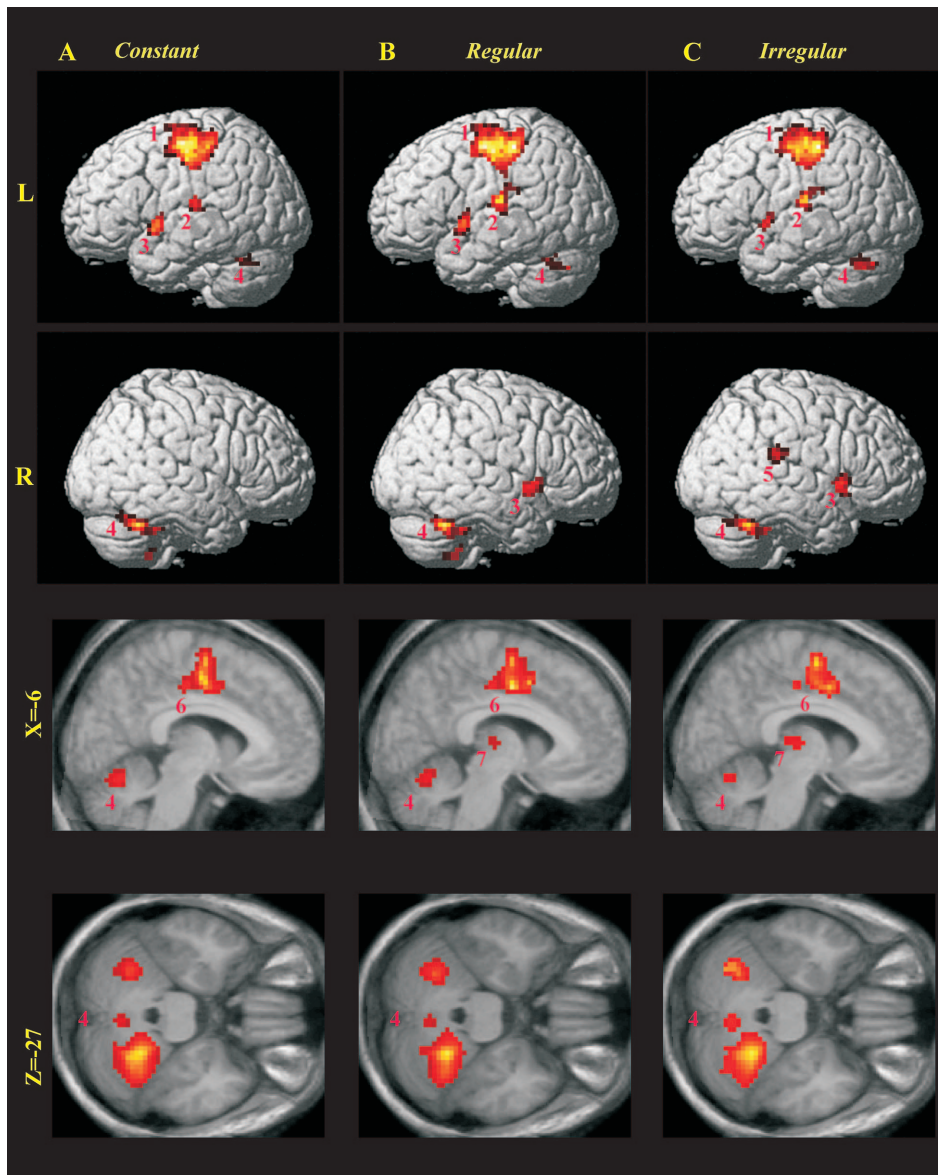


FIG. 5. Significant increases in the blood-oxygen-level-dependent (BOLD) contrast signal ($P < 0.05$ corrected) when constant (A), regular (B), and irregular (C), respectively, were contrasted against the rest condition. All conditions were associated with activation patterns in the frontal and parietal lobes and the cerebellum. *Top 2 rows*: a render image of the left and right hemisphere, respectively; *bottom 2 rows*: sagittal and axial slices of a mean anatomical image compiled for 6 of the subjects. 1, primary somatosensory cortex (S1)/primary motor cortex (M1) and dorsal premotor cortex (PMD); 2, parietal operculum; 3, lateral fissure; 4, cerebellum; 5, supramarginal gyrus; 6, supplementary motor area (SMA) and cingulate sulcus (CMA); 7, thalamus. See Table 1 for details.

and the dorsal premotor cortex (PMD) in all conditions. In the left SMA, the cluster of active voxels was located mainly posterior to the vertical plane at $y = 0$, which corresponds to SMA proper according to Picard and Strick (1996). These clusters extended rostrally into the putative pre-SMA and ventrally into the CMA. In the cerebellum all conditions engaged the cerebellar hemispheres bilaterally.

Brain activation: regular minus constant and irregular minus constant

The comparison regular minus constant revealed an increased activation in the left postcentral sulcus, the left cerebellar hemisphere, the left thalamus, and in the left parietal operculum ($P < 0.05$ corrected; Table 2 and Fig. 6A). At $P < 0.001$ uncorrected, an activation was observed in the right inferior frontal gyrus pars opercularis (area 44) and the left inferior part of the precentral sulcus.

The comparison irregular minus constant revealed increased activation in the right supramarginal gyrus, the right inferior

frontal gyrus pars opercularis (area 44; $P < 0.05$ corrected), and the left parietal operculum ($P < 0.001$ uncorrected; Table 2 and Fig. 6B).

A conjunction analysis was made to determine the cortical areas that were more strongly activated in both regular and irregular as compared with constant. The result of this analysis was consistent with the results present in the preceding text. Activations were observed in the left parietal operculum, the right supramarginal gyrus, the right inferior frontal gyrus pars opercularis (area 44), and the left thalamus ($P < 0.05$ corrected; Table 3 and Fig. 7). At $P < 0.001$ uncorrected activations in the left lateral and medial cerebellum, the left inferior part of the precentral sulcus (border zone between areas 44 and 6) and the left supramarginal cortex were also found. Thus the engagement of the inferior frontal cortex and supramarginal cortex appears to be bilateral. The BOLD signals in these, and some other relevant areas, are plotted in Fig. 8. Stronger activation was observed in irregular and regular as compared with constant in the left parietal operculum, left thalamus, and

TABLE 2. *Task specific activations*

Anatomical Region	Talairach Coordinates			Peak z Score	Cluster Size ³	P Value
	x	y	z			
Regular versus constant						
Left parietal operculum	-57	-18	15	3.79	7	0.026 ¹
Left ventral thalamus	-12	-18	6	3.85	6	0.035 ¹
Left lateral cerebellum (Lobule VI)	-24	-60	-27	3.37	10	0.012 ¹
Left postcentral sulcus	-51	-30	54	3.44	5	0.047 ¹
Left inferior precentral sulcus (Area 44/area 6)	-60	6	15	3.60	11	<0.001 ²
Right inferior frontal gyrus/pars opercularis (BA44)	57	15	6	3.35	5	<0.001 ²
Irregular versus constant						
Right supramarginal gyrus	57	-33	30	3.72	67	0.010 ¹
Right supramarginal gyrus	66	-33	24	3.50	9	0.017 ¹
Right inferior frontal gyrus/pars opercularis (BA44)	54	12	0	3.79	13	0.007 ¹
Left lateral fissure	-54	15	-6	3.71	12	<0.001 ²
Left parietal operculum	-57	-21	18	3.38	10	<0.001 ²
Irregular vs regular						
Right inferior frontal gyrus/pars opercularis (BA44)	54	18	-3	3.51	9	0.042 ¹
Left lateral fissure (right anterior insular cortex)	-39	18	-3	3.39	15	<0.001 ²
Regular versus irregular						
Right precentral gyrus (PMD)	45	-12	54	4.24	34	0.026 ¹

¹ Corrected *P* values using a small volume correction. ² *P* < 0.001, uncorrected. ³ Number of cubic 27 mm³ voxels in cluster.

right supramarginal cortex. In addition, there was a step-wise increase in activity in the right inferior frontal gyrus when going from constant to regular, and regular to irregular. As a control, no BOLD signal change was found in a peak situated in the central sulcus, equally activated throughout the three experimental conditions.

Brain activation: irregular minus regular and regular minus irregular

The right inferior frontal gyrus pars opercularis was more strongly activated in the irregular condition than in the regular condition (Table 2 and Fig. 6C). In contrast, the right precentral gyrus (PMD) showed increased activity when we contrasted regular minus irregular (Table 2).

DISCUSSION

The present study emphasizes the role of three cortical regions in the programming of the fingertip forces during weight changes in a precision grip lifting task: the left parietal operculum, the bilateral supramarginal gyrus, and the bilateral inferior frontal cortex. By varying the need to update the sensorimotor representation of object weight and to apply corrections in different lifting conditions, we could show an increased involvement of these cortical regions.

Mechanisms for object manipulation

The behavioral results obtained during the MR scanning corresponded well with the model of precision grip manipulation presented in the introduction (Fig. 1). During the constant condition, when the same weight was lifted in consecutive lifts, subjects generated a well-programmed motor output that was targeted to the weight of the object. Thus there was no mismatch between the predicted and afferent sensory information. As such, there was no need for corrective adjustments to be made and no need to update the sensorimotor memory representation. During the regular condition, the subjects pro-

grammed the force output close to the heavy and light target, respectively. Thus they shifted from one object representation (heavy) to the other (light) after each lift. But as the scaling effect of the peak force rate to the object rate was smaller than for the constant condition, there was a slight mismatch that generated small corrective force adjustments. During the irregular condition, subjects could not predict the weight changes. Most of the subjects adopted a strategy in which they programmed the motor output between the two weights with a clear bias toward the heavy weight. A similar safety strategy for randomly presented weights has been described previously (Gordon et al. 1991). In both heavy and light lifts, subjects performed an inappropriate programming, which resulted in either the lift off occurring sooner than expected (when the weight was lighter), or no lift off taking place when expected (because the object was heavier than predicted) (see Gordon et al. 1993). Both of these unexpected events are known to trigger prestructured reactive motor commands that result in either a fast termination or a brisk increase of the force output within 100 ms (Johansson and Westling 1988; Westling and Johansson 1987). The memory of the previous lift has previously been shown to be a powerful factor that influences the anticipatory scaling of fingertip forces in precision grip lifting tasks (Edin et al. 1992; Jenmalm and Johansson 1997; Johansson and Westling 1988). At present, only sparse knowledge exists about the time characteristics of the memory representations of object properties that are used to set the parameters in the grip-lift motor program (see Gordon et al. 1993). Yet we know that these memory representations can be swiftly updated between subsequent lifts (Johansson and Westling 1988). Although most subjects in the present study adopted a safety strategy in which they programmed the forces close to those appropriate for the heavy weight, the anticipatory parameter control was used in the irregular series to update the internal representation between each lift. This was evident by the small differences depending on which weight had just been lifted (Fig. 4B).

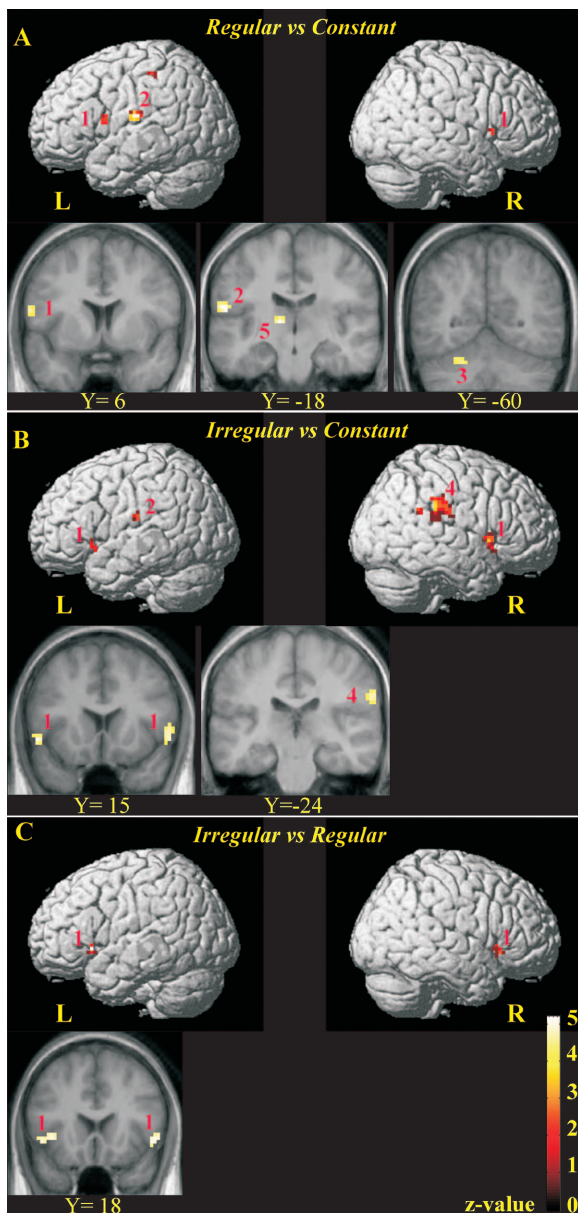


FIG. 6. Brain regions significantly more activated during the regular as compared with the constant condition (A), during the irregular as compared with the constant condition (B), during the irregular as compared with the regular condition (C). *Top*: from left to right, render images of the left and right hemispheres. *Bottom*: coronal slices showing the location of increased activations superimposed on a mean anatomical image of 6 subjects. 1, inferior frontal gyrus (pars opercularis); 2, parietal operculum; 3, cerebellum; 4, supramarginal gyrus; 5, thalamus. For details, see Table 2.

In summary, the behavioral analysis validated the design of our experiment. In the first constant condition, there was a well-programmed force output with no need for corrections to be made or for updating of the sensorimotor memory representation of the object. In the regular condition, there was a change in the sensorimotor representation between each lift attributed to updating. In spite of this, there was still a small error in the programming of the lift, generating a small sensory mismatch and some corrective force adjustments. Finally, in the irregular condition, the motor output was erroneously programmed in most lifts, generating a large mismatch, significant corrective force

adjustments, and updating of the sensorimotor memory representation of the object's weight.

Fronto-parietal activity associated with sensorimotor representations

When compared with the resting condition, the three lifting conditions activated a bilateral fronto-parietal network that was similar to the active networks observed in previous precision grip (Ehrsson et al. 2000, 2001, 2003) and tactile exploration studies (Binkofski et al. 1999; Seitz et al. 1991). The key novel finding in the present study is that some regions within the bilateral fronto-parietal network were more active in the regular and irregular conditions as compared with the constant condition. These differences could not be due to differences in the amplitude of the force, the number of lifts or the frequency of lifts because these were similar in all three conditions. According to the behavioral analysis, the regular and irregular conditions engaged the anticipatory parameter control and the sensory driven control to a greater extent than the constant condition. Hence, the changes in neural activity in the right inferior frontal gyrus, the right supramarginal gyrus, the left parietal operculum, and the left thalamus seem to be specifically involved in the sensorimotor processes leading to corrective reactions and updating of the memory representation of the object's weight. That the inferior frontal gyrus takes part in the sensory-driven control policy is further strengthened by the fact that it was more active during the irregular condition than during the regular one.

Inferior frontal cortex

The increased activity in the inferior frontal gyrus during the irregular condition probably reflects the discrepancy between the predicted and the actual sensory input and/or the subsequent neural processing to correct the ongoing movement and update the sensorimotor memory representation. The inferior frontal cortex might influence the fingertip force output via its extensive anatomical connections to the primary motor cortex (Godschalk et al. 1984; Kurata 1991; Matelli et al. 1986) or via direct cortico-spinal projections (Dum and Strick 1991). It can also receive tactile and kinesthetic information about the weight of the object and slips at the finger-object interface via projections from somatosensory areas in the parietal lobes, including the parietal operculum (Cipolloni and Pandya 1999; Ghosh and Gattera 1995; Preuss and Goldman-Rakic 1989). Of interest is the specific location of the frontal activity to the most ventral part of area 44 (see RESULTS). At $P < 0.001$ uncorrected, an activation was also observed in the left inferior frontal cortex, suggesting a bilateral engagement of this region. The human inferior frontal cortex is known to be active during object manipulation with the precision grip (Ehrsson et al. 2000, 2001) and during manual exploration (Binkofski et al. 1999). Likewise, in macaque monkeys a similar region is active when they grasp objects using precision grip (Rizzolatti et al. 1988). The inferior frontal cortex thus seems to contain a representation of skilled finger actions in both human and non-human primates. This representation does probably not represent lower level aspects of the finger movement such as muscles and forces but rather higher-order aspects of the movement such as grasp gesture (precision or power grip)

TABLE 3. Activations found by conjunction analyses between regular changes versus constant weight and irregular changes versus constant weight

Anatomical Region	Talairach Coordinates			Peak z Score	Cluster Size ³	P Value
	x	y	z			
Left parietal operculum	-57	-21	18	5.64	109	<0.001 ¹
Left thalamus	-12	-18	9	4.91	236	0.023 ¹
Left ventral thalamus	-6	-18	6	4.08		0.026 ¹
Right inferior frontal gyrus/pars opercularis (Area 44)	57	12	0	4.09		0.025 ¹
Left inferior precentral sulcus (Area 44/area 6)	-57	9	15	4.25	37	<0.001 ²
Right supramarginal gyrus	66	-30	24	3.96	67	0.040 ¹
Left supramarginal gyrus	-51	-30	33	3.75	49	<0.001 ²
Left intraparietal cortex	-27	-42	69	3.62	8	<0.001 ²
Left lateral cerebellum (Lobule VI)	-36	-63	-30	4.25	17	<0.001 ²
Left medial cerebellum (Lobule V)	6	-60	-24	3.62	5	<0.001 ²
Right precentral sulcus (PMD)	42	3	54	3.36	11	<0.001 ²

¹ Corrected *P* values using a small volume correction. ² *P* < 0.001, uncorrected. ³ Number of cubic 27 mm³ voxels in cluster.

(Ehrsson et al. 2000; Rizzolatti et al. 1988), the spatial pattern of the movement (Kakei et al. 2003; Schwartz et al. 2004), and action goal (Rizzolatti et al. 1988). Neuronal populations in the inferior frontal gyrus are also activated when monkeys (Rizzolatti et al. 1996) and humans (Buccino et al. 2001; Heiser et al. 2003; Iacoboni et al. 1999; Nishitani and Hari 2000) observe goal directed hand actions and when humans imagine hand actions (Binkofski et al. 2000; Decety et al. 1994; Ehrsson et al. 2003); this is consistent with the view that the action representation in the inferior frontal cortex reflects higher-order aspects of movement. In the present study, predictable and unpredictable weight changes of an object during a lifting task were associated with increased synaptic activity in the inferior frontal gyrus. This might indicate that the role of the inferior frontal cortex is to process and store information about the physical properties of external objects and use this information to set the parameters of the motor programs used for object manipulation.

Parietal lobe

The lateral part of the left (contralateral) parietal operculum showed increased activity during the two conditions in which the weight of the object changed in the lifting series as compared with the constant lift. Previous studies have shown

that the parietal operculum contributes to somatosensory processing in humans (Burton et al. 1993; Disbrow et al. 2000; Ledberg et al. 1995). In non-human primates, several somatosensory fields have been described in this region (Krubitzer et al. 1995; Robinson and Burton 1980a,b). The parietal operculum is activated in various manipulative tasks including precision grip (Ehrsson et al. 2000, 2001, 2003; Kuhtz-Bushbeck et al. 2001) and manual exploration of objects (Seitz et al. 1991). One cause of the increased activity in the parietal operculum could be increased afferent somatosensory inputs related to slips occurring during erroneous grip force programming. However, our force recordings could reveal no slips either in the regular or in the irregular condition. Yet small corrective force adjustments took place both in the irregular and regular conditions, whereas no such adjustments occurred in the constant condition. The somatosensory signals associated with these adjustments could be one source of the increased parietal activity. However, there was no activation (even when the threshold was lowered; *P* < 0.01 uncorrected) detected in the primary somatosensory or motor cortices; this would be expected if the activation in the parietal operculum was due to an increased afferent somatosensory input. Another explanation for the parietal opercular activation, getting some support from previous studies, is that it reflects somatosensory information about the weight *change* of the object. An earlier fMRI study

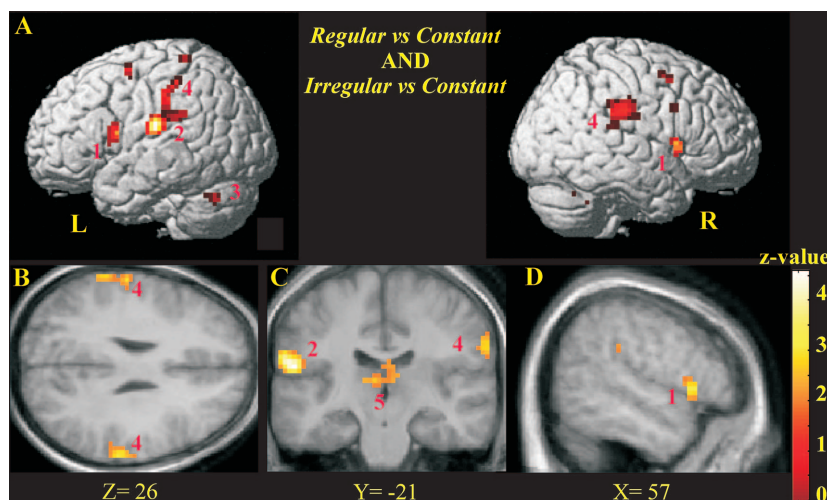


FIG. 7. Brain regions significantly more activated during the regular and irregular conditions as compared with the constant condition as revealed by the conjunction analysis (regular–constant and irregular–constant) (*P* < 0.05 corrected for multiple comparisons). *Top*: from left to right, render images of the left and right hemispheres (A). *Bottom*: axial (B), coronal (C), sagittal (D) slices showing the location of increased activations superimposed on a mean anatomical image of 6 subjects. 1, inferior frontal gyrus (pars opercularis); 2, parietal operculum; 3, cerebellum; 4, supramarginal gyrus; 5, thalamus. For details, see Table 3.

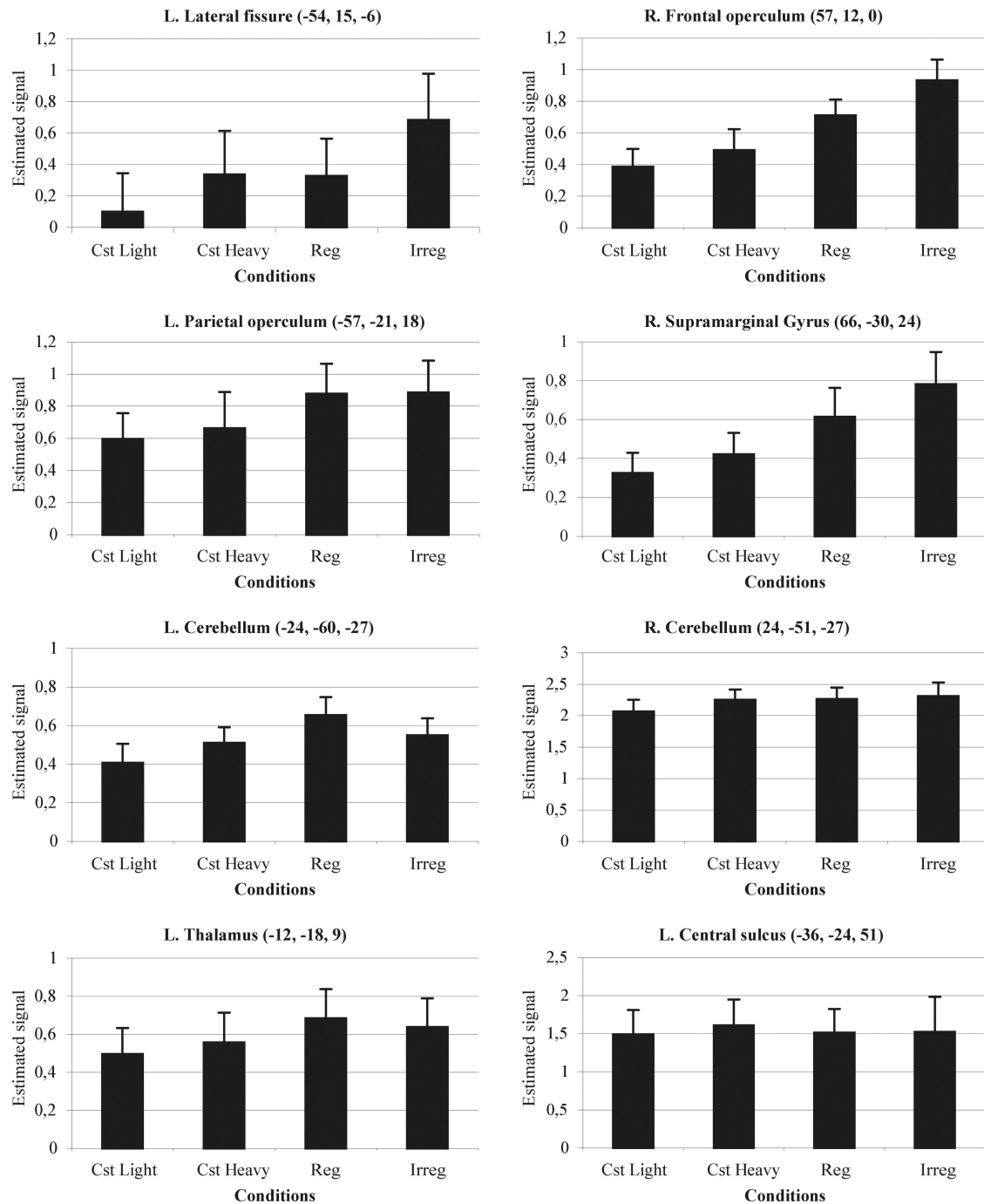


FIG. 8. Parameter estimates for the local maxima of the frontal (left lateral fissure and right inferior frontal gyrus) and parietal (left parietal operculum and right supramarginal gyrus) regions, the cerebellum, the thalamus and the central sulcus for the 3 conditions (the constant condition was divided into constant light and constant heavy) against rest.

has shown that activity in the lateral inferior parietal cortex reflects unpredictable changes in tactile stimulation (Downar et al. 2000), and neuronal recordings in monkeys have shown that cells in SII has the capacity to maintain somatosensory information over several seconds to facilitate the discrimination between two sequential stimuli (Romo et al. 2002). The parietal operculum has neuroanatomical connections with a wide number of both primary and nonprimary sensorimotor areas including the inferior frontal cortex and the inferior parietal cortex (area 7b, which might correspond to the supramarginal

gyrus in humans) (Cipolloni and Pandya 1999; Disbrow et al. 2003; Ghosh and Gattera 1995; Matelli et al. 1986; Pandya and Kuypers 1969; Preuss and Goldman-Rakic 1989). Thus the parietal operculum might convey the critical somatosensory feedback from the fingertips to a fronto-parietal network including the inferior frontal and the supramarginal cortices that control the fingertip forces during object manipulation.

In a previous study, we found activity in the right intraparietal cortex that seemed to reflect the predictive grip force increase providing grasp stability during an isometric grip-lift

task (Ehrsson et al. 2003). Unexpectedly, we did not observe an activation of this section of the right intraparietal cortex when we contrasted the lifting tasks with rest in the present study ($P < 0.01$ uncorrected). Instead we found parietal activity in the right supramarginal cortex and in the most anterior part of the left intraparietal cortex ($P < 0.001$ uncorrected). This difference could be due to the fact that different sections of the frontal, parietal and cerebellar areas are used for different skilled hand actions (e.g., Ehrsson et al. 2000; Imamizu et al. 2003), reflecting the various sensorimotor transformations involved.

Complementary role of the cerebellum

We found cerebellar activations in the bilateral hemispheres and right vermis during all lifting conditions, well in agreement with the central role of the cerebellum in the control of skilled motor actions (see also Kinoshita et al. 2000). In our previous fMRI experiments, exploring brain activity during precision grip (Ehrsson et al. 2000, 2001, 2003), the field of view of the scanner was restricted, which means that the cerebellum was not scanned.

A key function of the cerebellum is to predict the sensory consequences of movement (Blakemore et al. 2001). Patients with cerebellar atrophy show changes in the timing and magnitude of the applied grip forces during object manipulation that support the role of cerebellum in anticipatory control (Babin-Ratté et al. 1999; Nowak et al. 2002). Convergent observations have suggested that the cerebellum, together with the parietal cortex, also may play a role in the process of on-line correction (for review, see Desmurget and Grafton 2000). If the cerebellar activations were reflecting the rapid corrective grip force corrections that occurred in the irregular condition, we would have expected the strongest activation in this condition. However, there was no significant difference between the irregular and regular conditions in this region. Depending on whether the weight is lighter or heavier than expected, the corrections are not the same and they are probably not subserved by the same areas. Because both events (lighter than predicted, or heavier than predicted) were mixed in the irregular condition, our design did not allow this distinction.

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