Motor Cortex Activation Is Related to Force of Squeezing

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Abstract: Primate studies have demonstrated that motor cortex neurons show increased activity with increased force of movement. In humans, this relationship has received little study during a power grip such as squeezing, and has previously only been evaluated across a narrow range of forces. Functional MRI was performed in eight healthy subjects who alternated between rest and right hand squeezing at one of three force levels. During scanning, motor performances were recorded using a dynamometer. At each force level, activation volume was measured within left sensorimotor cortex, right sensorimotor cortex, and a midline supplementary motor area. In left sensorimotor cortex, % signal change was also assessed. The range of force generated across the three force levels varied from 4.9 N to 276 N. In left sensorimotor cortex, activation volume increased significantly with greater force. The % signal change also increased with greater force and correlated closely with activation volume. In supplementary motor area, activation volume increased significantly with increasing force, but with greater intersubject variability. In right sensorimotor cortex, a trend for larger activation volumes with greater force did not reach significance. The laterality index, an expression of the relative degree of contralateral vs. ipsilateral sensorimotor cortex activation, did not change across the three force levels. Increased force of squeezing is associated with increased contralateral sensorimotor cortex and supplementary motor area activation. This relationship was found across the full spectrum of forces that the human hand is capable of generating. Use of a valid, reliable method for assessing motor behavior during functional MRI may be important to clinical applications. *Hum. Brain Mapping* 16:197–205, 2002. © 2002 Wiley-Liss, Inc.

Key words: functional MRI; grip force; human; dynamometer; motor cortex

INTRODUCTION

Primate studies have provided evidence that motor cortex activity is related to several features of movement, including movement displacement, preparation, velocity, position, and force [Ashe, 1997; Fetz, 1994; Humphrey et al., 1970]. One aspect that has received considerable attention is the relationship between magnitude of force and neuronal activity in primary motor cortex. A number of tasks have been evaluated in this regard, most involving the distal upper extremity. There is general agreement that many cells increase activity with increasing force [Belhaj-Saif, et al., 1996; Cheney and Fetz, 1980; Evarts, 1968; Hepp-Reymond et al., 1978; Hoffman and Lus-

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chei, 1980; Jennings et al., 1983; Maier et al., 1993; Muir and Lemon, 1983; Tanji, 1975; Thach, 1978]. Some studies have suggested that some primary motor cortex neurons are more responsive to a precision grip such as pinching, as compared to a power grip such as squeezing [Muir and Lemon, 1983].

Several human brain mapping studies have examined the relationship between brain activation and generation of graded force. Increased force has been associated with regionally increased activation in some [Dettmers et al., 1995; Ehrsson et al., 2000; Thickbroom et al., 1998] but not other [Ludman et al., 1996; Wexler et al., 1997] studies. Each of these studies employed a different motor task to activate the brain, possibly accounting for divergent conclusions. Each study, however, employed only a small range of force, and all but one study was restricted to use of a precision grip. One goal of the current study was to probe the relationship between force and motor cortex activity in humans during use of a power grip, such as squeezing, and to do so over a much broader range of human hand forces.

Accurately measuring the force of the hand movements is central to a study of this sort. Previous studies have used divergent methods, including an isometric key press [Dettmers et al., 1995], a wooden lever connected to a rubber band [Wexler et al., 1997], an optic transducer system [Ehrsson et al., 2000], and a sphygmomanometer bladder [Thickbroom et al., 1998]. Some of these devices employ a nonlinear scale. Others measure pressure instead of force and are thus sensitive to variations in the surface area of hand contact. One of the goals of the current study is to evaluate a method for measuring motor performance that addresses these concerns. We have previously employed a method to measure motor performance at the bedside [Cramer et al., 1997a; Nelles et al., 1998], where it was found to be sensitive, valid, and reliable. This method was evaluated during fMRI.

The current study aimed to evaluate activation in three motor cortex regions during generation of graded levels of force during squeezing, and to compare precise measures of squeezing force with features of brain activation. Squeezing was also of interest because of its potential as a probe of motor function in patients with neurological disorders. Squeezing can be performed by subjects with motor deficits [Brunnstrom, 1970; Twitchell, 1951] and thus has been used in several previous clinical brain mapping studies [Cramer et al., 2001; Honda et al., 1997; Lee et al., 1998; Schlosser et al., 1997].

MATERIALS AND METHODS

Subjects and training

Eight right-handed [Oldfield, 1971] healthy subjects with no history of neurological disease were recruited. Each had a normal neurological exam and no active or previous significant neurological disease. Each signed a consent form approved by the Institutional Review Board of the Massachusetts General Hospital.

Before scanning, each subject was briefly trained in motor task performance. Each was asked to squeeze a force transducer with the right hand. The force transducer (SSM-AJ-50, Interface Scottsdale, AZ) was made of aluminum and was fitted with two curved plastic handles. Transducer dimensions are $9 \times 8 \times 3$ cm, with a grip circumference of 18 cm. The transducer was held in the palm, with squeezing performed by four fingers on the top handle of the transducer and the thumb on the bottom handle of the transducer. An auditory metronome was used to cue movements at 1 Hz. Squeezing was performed at three levels of force: light (L), medium (M), and hard (H). Each subject individually defined these levels. Subjects were only asked to modify performances if M was not at least 50% greater than L, or H was not at least 50% greater than M. Thus, before scanning, each subject was able to demonstrate consistent repetitive squeezing at three separate force levels. The maximum force of squeezing by the right hand was also recorded. Pre-scanning training took less than 10 min in each case.

MRI image acquisition

Functional and conventional images were obtained using a quadrature head coil and a whole body 1.5 Tesla General Electric Signa scanner modified for echo planar imaging (EPI) by Advanced NMR Systems. Head movement was minimized with foam rubber pads and a restraining Velcro band across the forehead. Body movement was limited by placement of a proximal strap across the arms. Arms were kept extended at the subject's side with minimal elbow flexion at all times. Each scanning session included: 1) high resolution volumetric images, 2.8 mm thickness; 2) high resolution EPI anatomical images in plane with functional images; and (3) three datasets of blood oxygenation level dependent contrast functional images, consisting of asymmetric spin echo images for T2* signal change, with TR of 1.5 sec, TE of 70 msec, effective field of view of 20 cm², and in-plane resolution of 3.1 mm². The entire cerebrum was imaged using 12 contiguous axial slices of 7 mm thickness.

Each dataset of functional images took 3.2 min and provided 128 images/slice, 60 during squeezing plus 68 during rest, for a total of 384 images/slice across all three functional imaging datasets.

During acquisition of each functional dataset, subjects alternated between 15-sec epochs of rest (r) and 15-sec epochs of 1 Hz squeezing at one of the three force levels. The rate of squeezing was guided by a 1 Hz metronome beep, presented through headphones continuously through all epochs. To minimize the effects of fatigue, the shortest possible epoch length was used. Previous studies indicate that signal change drops off sharply at epoch lengths of 10 sec or shorter [Bandettini, 1999], so 15 sec was adopted. Because faster rate of movement is generally associated with increased signal [Rao et al., 1996; Schlaug et al., 1996], the fastest possible squeezing rate was used. Our preliminary behavioral studies found that head movement was increased at squeezing rates of 1.5 Hz and higher, so a 1 Hz squeezing rate was used. The cue to begin squeezing, as well as the level of force to be used for each epoch, was verbally announced through the headphones (e.g., "begin light squeezing"). Before this point, subjects only knew that they would be alternating between rest and squeezing at one of the force levels. The cue to stop squeezing was also announced verbally ("stop squeezing"). For each subject, the first fMRI dataset consisted of rLrMrHrHrMrLr. The second fMRI dataset consisted of rMrHrLrLrHrMr, whereas the third fMRI dataset consisted of rHrLrMrMrLrHr. Subjects kept eyes closed at all times. All movements were monitored for accurate performance by one of the experimenters standing in the scanner room at the subject's side.

Throughout functional imaging, subjects held a force transducer in the right hand, maintaining a consistent grip throughout the study, and allowing recording of squeezing performances. The force transducer was connected to a DC bridge amplifier (ETH-200, AD Instruments, Milford, MA) in the scanner room, which connected through a wall panel to an analog-to-digital converter (MacLab, AD Instruments) outside of the scanning room. The data were then recorded and displayed on a computer running strip chart-emulating software (Chart v. 3.5.1, AD Instruments). Data were collected along a continuous scale at 200 samples/sec. Before imaging, a linear measurement scale was confirmed by calibration with standard 0.1–1.0 kg brass weights. This method of motor assessment has been described in greater detail previously [Cramer et al., 1997a].

Data analysis

Head motion was detected and corrected using image registration software adapted for fMRI by Jiang et al. [1995]. To generate activation maps contrasting rest with each of the force levels, scans two and three were motion corrected to, then normalized to, the first scan of each subject. The three scans were then concatenated for each subject. Three sets of maps were generated, contrasting rest (204 images) with light squeezing (60 images), with medium squeezing (60 images), or with hard squeezing (60 images). Activation maps were generated voxel-by-voxel using a *t*-test. Identification of images as squeezing or rest was shifted by six seconds to account for the delay normally seen in the rise of cerebral blood flow (CBF) after neuronal activation [Cohen and Bookheimer, 1995]. Statistical maps were smoothed with a Hanning filter (FWHM 6 mm).

For each of the three statistical maps for each subject, measurements of activation were made within three regions of interest: the left sensorimotor cortex (SMC), the right sensorimotor cortex, and a midline supplementary motor area (SMA). These regions were parcellated using each subject's EPI high resolution anatomical images. Parcellation was guided by reliable sulcal landmarks [Ono et al., 1990] and a multiplanar radiological brain atlas [Damasio, 1995] while simultaneously viewing the volumetric images reformatted in the three cardinal planes. The SMA extended from pre-central sulcus to a rostral limit halfway between central sulcus and the anterior-most extent of the brain [Penfield and Welch, 1951], medially from brain vertex to cingulate sulcus, and laterally from mesial cortex on the left to mesial cortex on the right. A single midline region was used representing SMA from both hemispheres, as at the current resolution activation from right and left SMA often overlap. Sensorimotor cortex extended from pre-central to post-central gyrus, and from brain vertex to Sylvian fissure.

The number of significantly activated voxels was counted within each of the three regions of interest using a threshold of $P < 0.001$. Two other parameters were also assessed in the left sensorimotor cortex. First, the number of significantly activated pixels was counted using a signal change of 1.5% as a threshold; this threshold was selected because this level of signal change is commonly found in cortical motor regions during motor task performance [Porro, et al., 1996]. Second, a weighted mean % signal change was measured, restricting analysis to pixels with signal change $>1.5\%$. A laterality index was determined, defined as

(left SMC – right SMC)/(left SMC + right SMC) [Cramer et al., 1997b; Lee et al., 2000].

Dynamometer recordings were reviewed. First, the pre-scanning dynamometer assessments were reviewed to determine the maximum squeezing force for each subject. Next, the average rate of squeezing during fMRI was assessed for each subject, in Hz, to confirm that squeezing was performed at the desired frequency. Finally, the mean value for peak squeezing force during fMRI was determined for each subject at each of the force levels.

Statistics

A paired *t*-test was used for categorical comparisons of fMRI parameters at the different force levels, with significance set at $P < 0.05$. The Pearson correlation coefficient was used for linear regression analysis.

RESULTS

The mean age was 33 years (range 25–45). There were six females and two males. All subjects performed the motor tasks correctly during scanning, based on visual inspection during scanning and review of dynamometer recordings. Head motion was present during one of the three fMRI datasets in one subject. For that subject, only the two artifact-free fMRI datasets were normalized, concatenated, and analyzed as above.

Analysis of dynamometer recordings provided data on the rate and force of squeezing during fMRI scanning. MRI scanning produced negligible artifact in the dynamometer recording, and the dynamometer introduced no artifacts in the individual T2*-weighted brain images. The mean rate of squeezing across all subjects was 1.1 Hz rather than 1 Hz, an effect of the cassette player used to play the metronome tape. During the active epochs, each subject produced a brief squeeze in response to each metronome beep, with approximately half of the 1-sec cycle being at rest and half used for squeezing. Squeezes were remarkably consistent across epochs and subjects, with the same amount of time spent on the upslope and the downslope of each squeeze. The mean force among the eight subjects for light squeezing was 26.5 N (range 4.9–65.7), which was significantly different ($P < 0.0001$) from the mean value for medium squeezing, 83.3 N (42.1–170.5), which was different ($P < 0.0005$) from the mean value for hard squeezing, 183 N (100.0–276.4) (Fig. 1A). The forces assessed in the current study therefore range from 4.9 N to 276.4 N. For each subject, the force of medium squeezing was at least 50% greater than light,

and hard was at least 50% greater than medium. When expressed as the % maximum squeezing force, the mean values across subjects were 11%, 33%, and 74% for the three force levels, respectively.

Each of the three parameters measured in left SMC showed a significant relationship with level of force (Figs. 1,2). When activation volume was determined using a *t*-test threshold to define significant activation (Fig. 1B), all eight subjects showed activation at the lowest force level. Comparing L with M squeezing, increased activation volume was present ($P < 0.01$) and was seen in all eight subjects. Comparing M with H squeezing, increased in activation volume was seen ($P < 0.05$), and was present in seven of eight subjects. When activation volume was determined using a threshold based on % signal change, both the L–M and M–H comparisons remained significant ($P < 0.01$), with seven subjects showing an increased volume in each case. The mean % signal change in left SMC (Fig. 1C) increased in seven subjects when force increased from L to M ($P < 0.005$); the % signal change also increased in seven subjects going from M to H force ($P < 0.05$). Across the three force levels, the volume (threshold of $P < 0.001$) and the magnitude (mean % signal change) of activation in left SMC were significantly correlated ($r = 0.74$, $P < 0.0001$).

In the other two brain regions examined, activation volume was less strongly related to the level of force generated. In SMA (Fig. 1D), all subjects showed activation at the lowest force level, but only four of eight subjects showed an increased activation volume when force increased from L to M. When force increased from M to H, seven subjects showed an increased activation volume ($P = 0.057$). The change in SMA activation volume reached significance ($P < 0.05$) when L was compared to H. SMA activation was immediately anterior to the coronal plane defined by the precentral sulcus, and was not present in the pre-SMA. In right SMC (Fig. 1E), only five subjects showed activation when the force level was L, six subjects at M, and seven subjects at H. When force increased from L to M, three subjects showed an increased volume. When force increased from M to H, five subjects showed an increased volume ($P = 0.08$). Significant activation was rarely seen in other brain regions, including premotor cortex anterior to the central sulcus and basal ganglia.

The relationship between force exerted and left SMC activation volume (using a threshold based on *t*-test and $P < 0.001$) was also considered, treating force as a continuous variable, i.e., using the actual force measured during scanning rather than categorizing force as L, M, or H. To account for inter-subject

Figure 1.

Measures of force and brain activation are shown for each of the eight subjects, at each of the three force levels. **A:** Mean force exerted by each subject measured during fMRI scanning. **B:** Number of significantly activated pixels in left SMC, determined using a *t*-test threshold of $P < 0.001$. **C:** The weighted mean % signal change in left SMC for all pixels exceeding the % signal change threshold of 1.5%. **D:** Number of significantly activated pixels in SMA. **E:** Number of significantly activated pixels in right SMC. **F:** The volume of left SMC activation correlates significantly ($r = 0.50$, $P < 0.02$) with actual force, expressed as each subject's % of maximum force. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.005$, **** $P < 0.0005$.

differences, the force was expressed as a % of maximum force for each subject. In left SMC, this correlation was significant ($r = 0.50$, $P < 0.02$; Fig. 1F). In right SMC and SMA, a trend toward correlation did not reach significance ($0.05 < P < 0.1$).

The laterality index was not significantly different between the three force levels, the means being 0.61 for light squeezing, 0.72 for medium squeezing, and 0.71 for hard squeezing.

DISCUSSION

In the current study, squeezing with an increasing level of force was associated with increased activation

volume and increased signal change in the contralateral SMC. Increased force was also associated with larger activation volumes in SMA. Activation volumes were assessed across a very wide range of forces, up to 276 N.

The current findings in human contralateral SMC and SMA are concordant with previous primate studies. Several tasks have been used in primate studies to evaluate the relationship between force and neuronal firing rate in motor cortex. Most [Belhaj-Saif et al., 1996; Evarts, 1968; Hepp-Reymond et al., 1978; Jennings et al., 1983; Maier et al., 1993; Muir and Lemon, 1983; Tanji, 1975], but not all [Hoffman and Luschei, 1980], have employed the distal upper extremity. Most

Figure 2.

For Subject 6, activation images are shown on the left, and the squeezing record obtained during fMRI is shown on the right. The same two contiguous axial slices are shown for each force level. The color bar to the far left encodes the *P*-value for the *t*-test applied to each $3.1 \times 3.1 \text{ mm}^2$ pixel, contrasting rest with squeezing at each force particular level. For the squeezing record, the x-axis is time, with the subject squeezing at $\sim 1 \text{ Hz}$. The y-axis is force in kg, converted to Newtons by multiplying by 9.8. The mean force during light squeezing was 1.04 kg (10.2 N), during which

activation in left SMC was 14 pixels; in SMA, 10 pixels; and in right SMC, 5 pixels. The mean force during medium squeezing was 7.18 kg (70.4 N), during which activation grew in left SMC (27 pixels) and in SMA (21 pixels), but not in right SMC (4 pixels). The mean force during hard squeezing was 16.18 kg (158.6 N), during which activation grew in left SMC (81 pixels), SMA (50 pixels), and right SMC (26 pixels). The % signal change increased at each of the force levels. This subject's maximum squeezing force, obtained before scanning, was 23.6 kg (231.3 N).

studies have focused on relatively small forces, but the generation of larger forces similar to those employed in the current study has also been evaluated [Belhaj-Saif et al., 1996; Hoffman and Luschei, 1980]. There is general agreement that many cells increase activity with increasing force, though a few cells decrease activity, and in some studies neuronal activity reaches a plateau at a particular force level. Such findings have been described in contralateral primary motor cortex [Belhaj-Saif, et al., 1996; Evarts, 1968; Hepp-Reymond et al., 1978; Maier et al., 1993; Muir and Lemon, 1983], primary sensory cortex [Jennings et al., 1983; Salimi et al., 1999; Tanji, 1975], and to a lesser extent in SMA [Smith, 1979]. Muir and Lemon [1983], recording from pyramidal tract neurons in primates, found that performance of a power grip such as squeezing is less consistently related to level of contralateral motor cortex activity, as compared to a precision grip, though increased neuronal activity was still present with increased force of a power grip. The extent to which this observation relates to fMRI, in which output from a

wider range of cortical cells is measured, is uncertain. The current results suggest that in humans, a significant relationship exists between force of squeezing and motor cortex activation.

Increased force of squeezing correlated significantly with increased activation volume within contralateral SMC (Fig. 1B). The moderate correlation between activation volume and force ($r = 0.50$, Fig. 1F) is similar to the range of correlation coefficients found in primate studies comparing force generation and the firing rate of individual contralateral primary motor cortex neurons [Maier et al., 1993]. Other factors might explain some of the changes observed in cortical activation volume with increasing force level, including inter-subject differences in the force-cortical activity relationship and in the specific muscles employed by each subject. Furthermore, increased sensory feedback in the setting of increased squeezing force might also account for some of the measured changes in cortical activation [Fetz et al., 1980]. Within contralateral SMC, increased % signal change also correlated with in-

creased activation volume. An increase in % blood oxygenation level dependent (BOLD) signal with increased level of stimulus correlates in some systems with increased neuronal activity [Heeger et al., 2000]. This suggests that, with generation of graded levels of force, increased neuronal activity occurs and is simultaneously associated with recruitment of larger volumes of SMC.

There is limited agreement among previous human brain mapping studies that have compared force generation with motor cortex activation. The motor task in most previous studies was more related to a precision grip than a power grip, and, by virtue of the task employed, each evaluated a smaller range of force (2 N to 37 N) as compared to the current study (4.9 N to 276 N). Dettmers et al. [1995], using positron emission tomography, found that generation of stronger force from repetitive right index finger 1 Hz movements was associated with increased CBF in multiple brain areas including left SMC, SMA, and right SMC. Thickbroom et al. [1998] used fMRI to study left SMC activation during sustained generation of force by right hand four-finger flexion. Increased force was associated with an increased volume of activation in left SMC, with no effect on the % signal change. An fMRI study by Wexler et al. [1997] found that increased level of force generated during repetitive right index finger tapping was associated with a significant increase in the volume of activation globally, with no change identified within any specific brain region. Ludman et al. [1996] used fMRI to study brain activation during repetitive right hand four-finger flexion against one of two weights (2.4 and 14 N). Increased force of flexion was not associated with a change in brain activation. The use of different motor tasks across studies may be an important contributor to the differences in study findings. Of the above studies, Dettmers et al. [1995] had subjects generate the highest range of forces; current results are most concordant with these authors findings.

In the current study, measurements were made in primary SMC, representing precentral gyrus plus postcentral gyrus, whereas most primate studies have focussed on precentral gyrus. The reason for doing so is that performance of a simple motor task is associated with activation foci that span the central sulcus. For example, an fMRI study of finger tapping found that the largest activation focus in peri-Rolandic gyri spanned both precentral and postcentral gyri in 37 of the 42 control subjects evaluated [Cramer et al., 2000]. Furthermore, the postcentral gyrus is a significant source of corticospinal tract axons [Galea and Darian-Smith, 1994], and primate studies have found that

postcentral gyrus neurons also show increased firing rate with generation of increased levels of force [Jennings et al., 1983; Salimi et al., 1999; Tanji 1975].

Activation volume in SMA was significantly related to force level, consistent with the direct connections known to be present between SMA and spinal gray matter [Galea and Darian-Smith, 1994]. As compared to contralateral SMC, the relationship between volume of activation in SMA and level of force generated was weaker, with more variability between subjects (Fig. 1D). Activity in SMA may be greater during unpaced movements [Passingham, 1993], though multiple studies, including the current one, have found that SMA nevertheless is active during paced movements. A number of functions have been ascribed to the SMA in the generation of movement, including anticipation, motor task sequencing, and performance of a complex task [Marsden et al., 1996]. The relationship between level of squeezing force and activity in the SMA may be due to different levels of sensory signal reaching the SMA at different squeezing forces, changes in corticospinal activity arising in the SMA, or changes in cortico-cortical activity between SMA and primary motor cortex [Dum and Strick, 1991] at different squeezing forces.

Activation in right SMC was absent in three of eight subjects at the light force level, and in one of the subjects at the hard force level (Fig. 1E). A trend for increased right SMC activation volume with greater force did not reach significance, with greater force associated with increased right SMC activation volume in most subjects but decreased volume in others. These results are consistent with a previous study by Ehrsson et al. [2000], who found that performance of a power grip at lower force levels (20 N) was associated with sensorimotor cortex activation contralaterally more than ipsilaterally. The activation that was observed in right SMC might reflect movements by the left hand during intended squeezing by the right hand. For example, Dettmers et al. [1995] found electromyographic evidence for recruitment of left arm muscles during generation of high levels of force by the right index finger. Two factors argue against this as a major factor in the current study. First, in a previous non-MRI study in which the same force recording system was used to measure motor performances, movements in the left hand were measured in only 19% of control subjects during 1 Hz squeezing at maximum force by the right hand [Nelles et al., 1998]. Second, the laterality index did not change as a function of force, suggesting that the contribution of the right SMC to right hand squeezing is relatively constant across force levels, rather than being selectively

recruited at the higher force levels. This result is similar to the findings of Just et al. [1996], who found that bilateral language areas increased activation with increased difficulty of language task, with no change in the relative contribution of the right hemisphere. Nevertheless, the current study would have been improved if a specific measure of bilateral muscle recruitment had been obtained, either during scanning or off-line, such as during a prescan rehearsal.

Motor studies differ from functional imaging studies in many other systems in that the brain activity of interest relates to an efferent process that is potentially easy to measure. The force transducer used in the current study produced a record of motor output during fMRI and is useful for post-imaging analysis of motor performance. Careful monitoring of subject performance during brain mapping is important to studies of brain function and plasticity [Poldrack, 2000]. The current system employs a linear, continuous, and calibrated scale to measure force. In a previous study, measurements with this system showed concurrent validity with clinical measures of motor function [Cramer et al., 1997a].

Other approaches to measuring motor performance during fMRI have potential limitations. Studies that evaluate squeezing with a bulb measure pressure (force/area) rather than force, with results thus being influenced by variations in the area of hand contact. In addition, such devices may not employ a linear scale. The use of rubber bands for resistance achieves MRI-compatibility, but does not permit recording of movement force. Measuring the force of movement offers certain advantages, such as enabling a direct comparison between force exerted and features of brain activation (Fig. 1F). This issue may have particular importance in a clinical setting, as squeezing is useful for brain mapping in patients with stroke, multiple sclerosis, and other neurological disorders [Cramer et al., 2001; Honda et al., 1997; Lee et al., 1998; Schlosser et al., 1997].

In this study of normal control subjects, increased squeezing force by the right hand was related to increased activation volume and BOLD signal change within left SMC, and to increased activation volume in SMA. There was a large degree of variability between subjects. The force transducer used to measure force during scanning may have utility in studying squeezing by patients with neurological conditions characterized by a change in motor status over time.

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