Dorsal Premotor Cortex and Conditional Movement Selection: A PET Functional Mapping Study

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Grafton, S. T., A. H. Fagg, and M. A. Arbib. Dorsal premotor cortex and conditional movement selection: a PET functional mapping study. *J. Neurophysiol.* 79: 1092–1097, 1998. Positron emission tomography (PET) brain mapping was used to investigate whether or not human dorsal premotor cortex is involved in selecting motor acts based on arbitrary visual stimuli. Normal subjects performed four movement selection tasks. A manipulandum with three graspable stations was used. An imperative visual cue (LEDs illuminated in random order) indicated which station to grasp next with no instructional delay period. In a power task, a large aperture power grip was used for all trials, irrespective of the LED color. In a precision task, a pincer grasp of thumb and index finger was used. In a conditional task, the type of grasp (power or precision) was randomly determined by LED color. Comparison of the conditional selection task versus the average of the power and precision tasks revealed increased blood flow in left dorsal premotor cortex and superior parietal lobule. The average rate of producing the different grasp types and transport to the manipulandum stations was equivalent across this comparison, minimizing the contribution of movement attributes such as planning the individual movements (as distinct from planning associated with use of instructional stimuli), kinematics, or direction of target or limb movement. A comparison of all three movement tasks versus a rest task identified movement related activity involving a large area of central, precentral and postcentral cortex. In the region of the precentral sulcus movement related activity was located immediately caudal to the area activated during selection. The results establish a role for human dorsal premotor cortex and superior parietal cortex in selecting stimulus guided movements and suggest functional segregation within dorsal premotor cortex.

INTRODUCTION

Humans are remarkably adept at performing a repertoire of motor acts on the basis of learned sensory cues. A critical step in this behavior is the selection process that determines which particular movements will be executed for a particular cue. Evidence from lesion studies in nonhuman primates support the hypothesis that dorsal premotor cortex (PMd) is involved in integrating visual information with motor commands and could potentially serve as an area where this selection process is mediated (Halsband and Passingham 1985). Neurophysiological studies of the nonhuman primate brain establish that the PMd is involved in movement preparation and execution (Passingham 1993). Emerging evidence suggests anatomic and functional diversity in this area with rostral PMd more associated with planning or selection, and caudal PMd more related to on-line correction of movement or execution (see Wise et al. 1997 for review; Johnson et al. 1996; Preuss et al. 1996). Neural recordings of ''motor set'' activity during conditional motor learning support the notion that PMd is also involved in a more general process of nonstandard mapping of conditional stimuli to movements (see Wise et al. 1996). It is reasonable to hypothesize that this more abstract process of selection is also localized to more rostral PMd.

In humans, lesions to the dorsal premotor area lead to difficulties in learning motor gestures determined by arbitrary visual cues, with preservation of learning spatial tasks such as pointing to remembered target locations (Halsband and Freund 1990). Despite this strong clinical evidence, functional brain mapping studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have largely failed to identify premotor areas associated with conditional movement selection. Most imaging studies have used simple directional motor output (such as joystick movements) and localization has been primarily in parietal areas (Deiber et al. 1991). A notable exception is a recent study by Deiber et al, (1997) showing activation of dorsal premotor cortex during selection of directional joystick movements based on both spatial and ''nonspatial'' cues relative to a task with directionally fixed motor output. In the present imaging experiment, we extend this finding by examining the role of dorsal premotor area for movement selection with a stimulus response mapping in which the motor output was a type of grasp (power and precision grip) rather than a movement direction. This design was motivated in part by the human clinical studies of Halsband and Freund (1990) that emphasized the importance of dorsal premotor cortex for learning gestural motor behaviors. Movement execution versus rest was also evaluated to determine if the areas involved in selection were located rostral to those involved in execution.

METHODS

Subjects

Six normal, right-handed (Oldfield 1971) young adult subjects participated in the study after informed consent was obtained in accordance with USC's Institutional Review Board. The mean age was 24.3 (range 19–32) and the male:female proportion was 3:3.

Apparatus and tasks

Subjects were taught to perform specific grasping movements on a custom manipulandum shown in Figure 1. Each of three stations mounted on the apparatus consisted of a rectangular block

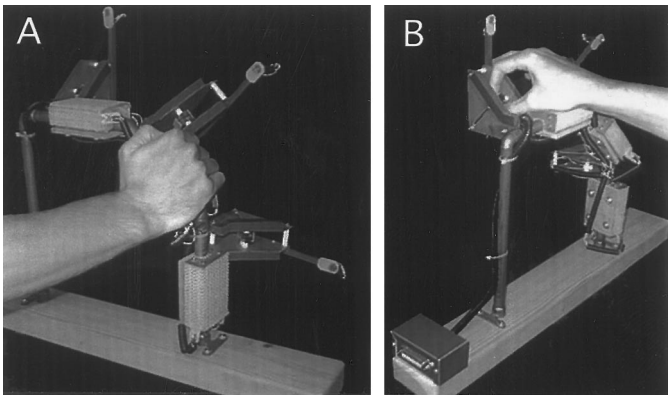

FIG. 1. Apparatus used in position emission tomography (PET) experiment. Each of 3 stations can be grasped in 2 ways: power grasp of block (*A*) or precision pinch of 2 plates in groove (*B*).

that could be grasped using a power grip (Fig. 1*A*) and a pair of plates mounted within a groove on the side of the block (Fig. 1*B*), which could only be grasped using a precision pinch (thumb and index finger). For a given station, the plates were positioned such that the wrist orientation remained the same for both grasps. Force sensitive resistor (FSR) material, mounted on the front and back of the blocks, detected when a solid power grasp had been established. The two plates were attached to a pair of mechanical microswitches, which detected when a successful precision pinch had been executed. A bicolored LED at each station was used: *1*) to provide feedback when a successful grasp was performed (change of color); *2*) to give imperative instruction indicating the next station to grasp (simple reaction task); and *3*) to indicate which type of grasp to use in a choice reaction task (conditional task only, see below). Once a successful grasp of a target was achieved, the subjects sustained the grasp position until a target above another station was given. For all tasks, 30 targets were presented every 3 ± (SD) 0.1 s in random order (90 s total).

Experimental conditions

POWER TASK. Subjects performed only power grips to the indicated blocks, irrespective of the LED color (Simple reaction task).

PRECISION TASK. Subjects performed only precision pinches to the indicated blocks, irrespective of the LED color (Simple reaction task).

CONDITIONAL TASK. Subjects performed a power grasp or precision pinch, depending on the LED color (red = power, green = precision). The LEDs were illuminated in random order. (Choice reaction task)

REST TASK. Subjects held their arm stationary in a power grip on the middle station throughout the scan and looked at each LED as it appeared.

Subjects practiced the grasping tasks for 5 min before scanning. Each of the four tasks was performed in triplicate in random order. The instructional cues were well-learned before scanning.

Performance analysis

Reaction time data were collected by a control computer (Macintosh PowerBook 140). Trial reaction interval, the time between each stimulus presentation and completion of movements, could be broken down into two component reaction times: *1*) the release time (time between stimulus presentation and release of manipulandum) and *2*) the depress time (the interval between stimulus presentation and grasp of new target plus 200 ms. The ''detection of the button press'' required that the subject hold the switch for 200 ms to ensure a secure press). The depress time was largely dependent on transport and preshaping of the hand to match target.

Imaging

Imaging methods have been described in detail previously (Winstein et al. 1996). In brief, relative regional cerebral blood flow (rCBF) images were acquired by using a modified autoradiographic method (Herscovitch et al. 1983; Raichle et al. 1983) with an intravenous bolus of 35 mCi of $H_2{}^{15}O$ commensurate with the start of scanning and the behavioral task. A 90 s scan was acquired and reconstructed by using calculated attenuation correction. A Siemens 953/A tomograph with 31 contiguous planes covering a 105-mm field of view and a nominal axial resolution of 4.3 mm at full width half maximum (FWHM) was used.

Image analysis

Image processing was performed on a SUN Ultra 1 workstation. For spatial normalization a within subject alignment of PET scans was performed by using an automated registration algorithm (Woods et al. 1998a). A mean image of the coregistered PET scans was coregistered to a population based PET reference atlas centered in Talairach coordinates using an affine transformation with 12 degrees of freedom (Talairach and Tournoux 1988; Woods et al. 1998b). Coregistered PET images were smoothed to a final isotropic resolution of 15 mm FWHM and normalized to each other by using proportionate global scaling.

The general linear model of multivariate analysis was used to calculate a 2-way analysis of variance (ANOVA) with repeated measures (task, subject, and repetition effects). Planned comparisons of task means were used to calculate the *t*-statistic between behavioral conditions on a pixel by pixel basis (Neter et al. 1990; Woods et al. 1996) with an uncorrected threshold of $P < 0.001$. Because our hypothesis concerned a small cortical area (left dorsal premotor and parietal cortex), a mask including only the left dorsal hemisphere was defined a priori and a critical *t* threshold ($t = 4.2$, corrected $P < 0.05$) necessary to account for multiple comparisons within this area was determined (Worsley et al. 1992). Peak sites on the *t*-map above the threshold were localized and maximal *t* and *P*-values at these sites as well as mean rCBF values for each task were tabulated. The resultant *t*-maps were superimposed on a reference MRI atlas from a normal subject centered in Talairach coordinates and rendered in three-dimensional perspective by using the display software AVS (Advanced Visualization Systems, Waltham, MA).

RESULTS

Performance

Choice reaction time tasks typically demonstrate significantly longer reaction times compared to simple reaction times. Performance measures of release and depress times in our study demonstrated a trend for responses to be slower under the conditional task, but this was not significant (Fig. 2). Unlike typical reaction time tasks that use ballistic movements, our tasks also required limb transport and prehension. This more complex movement execution likely obscured the delay associated with response selection. Error rates were less than 2% across the three trials of each task. There was no significant difference of performance across repetitions of the conditional task, confirming that learning of the stimulus-response mapping was established before scanning.

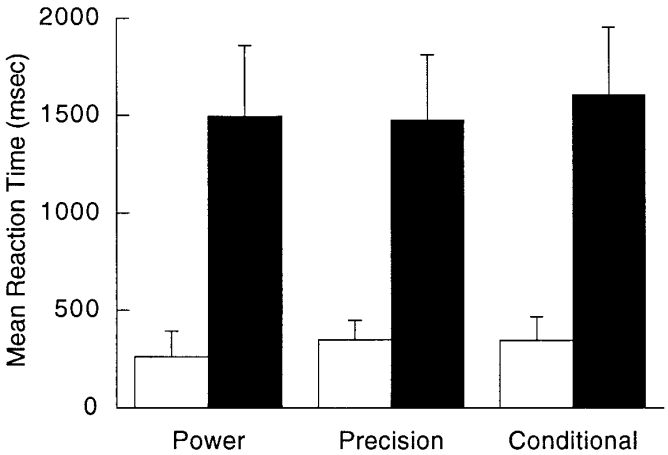

FIG. 2. Mean release time (white bar) and depress time (black bar) for 3 movement tasks. There were no significant performance differences between simple (power or precision) and choice (conditional) reaction tasks.

Conditional movement selection

The conditional movement selection task was compared with an average of the power and precision tasks. [conditional − (power + precision)/2]. Thus the average rate of producing power or precision type grasps was counterbalanced (with similar reaction times), reducing the contribution of movement planning, kinematics or direction. As shown in Fig. 3, the key finding is an activation of left rostral dorsal premotor cortex. Two additional sites are located in the left superior parietal lobule with one maximum located along the medial wall of the intraparietal sulcus. Anatomic localizations are summarized in Table 1.

Movement execution

Comparison of all three movement tasks with the rest task identified areas involved in executing visually guided movements. As shown in Fig. 3 and Table 2, a large contiguous activation was centered near primary motor cortex and extended into precentral gyrus (premotor cortex), mesial frontal cortex, and also postcentral gyrus (dorsal parietal cortex), concordant with many previously reported activation studies of arm movement versus rest. The activation in the left hemisphere can be seen to extend inferiorly along the precentral gyrus to one putative site for the ventral premotor cortex (Talairach coordinates -55, -7, 25, B.A. 6) (Winstein et al. 1996). Note that the location of the premotor site associated with grasp selection (in yellow) is at the rostral margin of, rather than entirely within, the movement related areas (in blue).

DISCUSSION

The main finding of this experiment was differential activation of dorsal premotor cortex and superior parietal cortex when subjects were required to make a selection of movement on the basis of arbitrary visual instructions. We used a forced choice selection task with nondirectional motor output, counterbalancing for movement preparation, direction, movement type and on-line feedback. The localization in PMd is consistent with clinical studies of patients with dorsal premotor lesions (Halsband and Freund 1990) and nonhuman lesion studies of PMd (Passingham 1993). The limited temporal resolution of PET does not allow us to link our findings with epoch specific behavior of single neurons recorded during motor set or motor preparation. Nevertheless, our findings are also consistent with the general hypothesis motivated by studies of motor-set that indicate that PMd is critical for learning nonstandard mappings based on visual stimuli (Wise et al. 1996).

Many previous imaging studies have identified motor-related functions in dorsal premotor cortex, including movement execution (Grafton et al. 1991, 1996; Roland et al. 1980), visually guided motor learning (Grafton et al. 1994; Kawashima et al. 1994), generating discrete finger movements (Larsson et al. 1996; Rao et al. 1993), motor sequence learning (Grafton et al. 1995; Jenkins et al. 1994), imagined movements (Stephan et al. 1995), consolidation of motor adaptation (Shadmehr and Holcomb 1997), and learning to resolve spatial stimulus response incompatibilities (Iacoboni et al. 1996). Although each of these tasks involve the movement selection process, they have not been designed to isolate the selection process from other movement related parameters. Preparatory related activity has been identified in prefrontal (Petrides et al. 1993) and parietal (Deiber et al. 1996) cortex and selection related activity in parietal cortex (Deiber et al. 1991; Kawashima et al. 1996). Only one imaging study designed specifically to examine the selection process has localized responses to premotor cortex (Deiber et al. 1997). In that study, nonspatial and spatial cues were used to indicate the direction of joystick movements. For both types of conditional stimuli there was an activation in premotor and parietal cortex compared to a task with fixed motor output. The location of their dorsal premotor site (Ta-

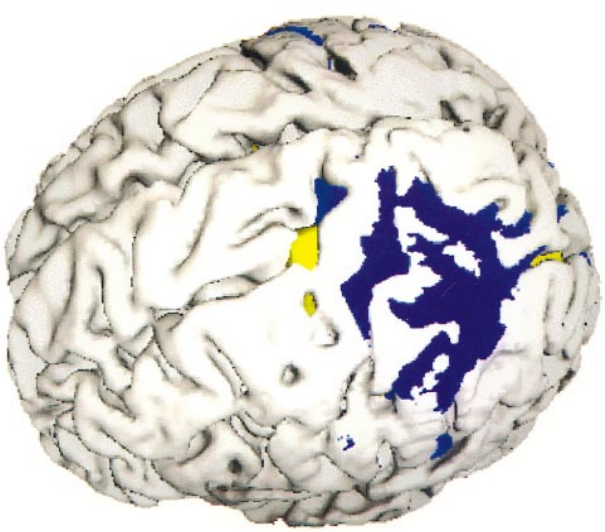

FIG. 3. Superior oblique view of left hemisphere demonstrating significant differences between execution (blue) and selection (yellow) tasks. Movement-related activity extends from primary sensorimotor cortex into adjacent precentral and postcentral, intraparietal sulcus and inferiorly along precentral gyrus to include ventral premotor cortex and a caudal portion of dorsal premotor cortex (PMd). Selection task activates superior parietal cortex and an area of PMd located at rostral margin of movement related area, suggesting functional separation within dorsal premotor cortex.

TABLE 1. *Localization of conditional selection of grasp*

Anatomic Region	Talairach Coordinates (mm)			Conditional Grasp		rCBF (ml/min/100 gm tissue)							
						Power grasp		Precision grasp		Rest			
	x	y	z	Average	St. dev.	Average	St. dev.	Average	St. dev.	Average	St. dev.	*t*-maximum	*P*-Value
L superior frontal sulcus (B.A. 6) Dorsal premotor cortex	−33	−3	48	72.96	4.19	70.44	3.55	70.77	3.61	70.94	5.66	4.20	0.0005
L superior parietal lobule (B.A. 7)	−25	−67	36	68.73	5.15	65.90	4.58	67.15	5.36	65.57	5.26	4.48	0.0001
L superior parietal lobule (B.A. 7)	−13	−63	49	69.89	3.08	67.10	2.86	68.28	3.65	67.72	3.97	4.45	0.0001
R occipital cortex (B.A. 17/18)	6	−94	7	69.24	4.45	66.03	4.30	67.23	2.31	65.10	4.18	4.90	0.00005

Significance determined by comparing conditional task with the 2 nonconditional tasks (power and precision). Mean flow values of rest condition are also included for comparison purposes. Test statistic corresponds to maximum *t*-value and corresponding *P*-value at each location. B.A., Brodmann's area as estimated by the Talairach atlas (Talairach and Tournoux 1988).

lairach -28, -12, 48) was located 10.3 mm caudal to the site identified in our study. Their experiment also identified a response in left superior parietal lobule (Talairach -16, -66, 44), within 5 mm of a site in the present study. The consistency of these two experiments suggests that the dorsal premotor and parietal areas are critical for movement selection irrespective of motor output (spatial or gestural).

We cannot exclude several alternative interpretations of our findings. Most importantly, the parietal and premotor changes could be the result of differences in attentional demands and or eye movements that would occur in a task requiring interpretation of visual cues versus a task with fixed responses. This is particularly problematic when we attempt to interpret activations in parietal and extrastriate cortex where attention has a strong modulatory effect. PET studies of directed visual attention do not detect changes at the premotor site we describe here (Corbetta et al. 1993; Nobre et al. 1997), arguing that the changes observed in our study and Deiber et al. (1997) are more likely to be related to the selection process. Differences in premotor cortex might also occur if motor performance varied between the variable and fixed responses. Electromyograph (EMG) data was not available to rule out differences in kinematics between the tasks. Nevertheless, observations of subjects performing these motor tasks reveal no consistent difference of behavior and it is doubtful that PET is sensitive enough to identify small variations of movement kinematics. Finally, any comparison of tasks where there is a difference in the number of possible responses for a given stimulus (irrespective of stimulus or response characteristics) might activate these areas.

In our study, the movement selection activity was located primarily in the precentral sulcus at the rostral margin of activity associated with movement. Execution related activity involved a larger expanse of postcentral cortex, central sulcus and precentral gyrus (i.e. premotor cortex) extending to the precentral sulcus. This spatial difference suggests a functional subspecialization within the dorsal premotor area with selection areas located rostral to execution areas, consistent with a similar gradation of function in nonhuman primates (Wise et al. 1997). In addition to premotor cortex, grasp selection activated a subset of parietal areas that were involved in movement execution. The two sites were in the superior parietal lobule (Brodmann's area 7). One of the responses was deep within the intraparietal sulcus, centered in the medial wall. If the intraparietal sulcus is used as a

TABLE 2. *Localization of movement related brain areas*

Anatomic Location	Talairach Coordinates (mm)			Conditional Grasp		rCBF (ml/min/100 gm tissue)							
						Power grasp		Precision grasp		Rest			
	x	y	z	Average	St. dev.	Average	St. dev.	Average	St. dev.	Average	St. dev.	*t*-maximum	*P*-Value
Left putamen/insula	−33	−7	16	69.2	2.6	70.4	2.6	70.1	2.1	67.4	2.1539	4.46	0.00005
L sensorimotor complex	−33	−27	55	77.7	4.2	77.8	4.2	76.3	4.1	66.9	2.2681	6.98	0.00000001
L occipital cortex (B.A. 18)	−4	−84	19	77.1	4.5	77.0	5.6	75.8	2.7	72.9	4.07	6.98	0.00000001
R inferior parietal lobule (B.A. 19)	22	−72	40	67.0	4.3	65.2	3.2	66.9	3.6	64.1	3.3251	4.49	0.00005
R sensorimotor cortex	33	−18	61	64.9	4.9	64.5	4.6	64.4	4.0	61.4	4.2441	6.35	0.0000001
R inferior parietal lobule (B.A. 40)	34	−39	51	70.3	2.9	70.4	2.7	70.0	3.1	67.6	2.892	5.50	0.00001
R inferior pareital lobule (B.A. 40)	58	−25	34	63.1	3.6	62.1	3.3	63.2	3.9	60.8	2.3776	4.93	0.00005

Significance determined by comparing 3 movement conditions (conditional, power, and precision) versus rest condition. Test statistic corresponds to the maximum *t*-value and corresponding *P*-value at each location. B.A. = Brodmann's area as estimated by the Talairach atlas (Talairach and Tournoux 1988).

reference, then it is possible that this area in humans is a functional homologue of the medial intraparietal area (MIP) described in nonhuman primates. In monkey, MIP receives visual inputs from extrastriate areas and projects directly to PMd. Functionally this area may be critical for merging visual, proprioceptive, and other information (Johnson et al. 1996). As the anatomic correspondence between human and primate parietal cortex is not fully established, other functional areas in nonhuman primates merit consideration. Neurons in area 5d of posterior parietal cortex have been associated with response selection in GO/NOGO tasks in monkey (Kalaska and Crammond 1995). For our grasping task there is another relevant site, the anterior intraparietal (AIP) area (Sakata and Taira 1994). In monkey, this area is located in the anterior portion of the lateral bank of the intraparietal sulcus, and contains neurons involved in matching grasp types with target attributes. Additional studies are required to establish functional and anatomic correspondence between human and nonhuman parietal domains. In the meantime, our results are consistent with a model of visuomotor control in which frontal and parietal cortex work in concert to select, prepare, and execute movements.

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