Signaling of Grasp Dimension and Grasp Force in Dorsal Premotor Cortex and Primary Motor Cortex Neurons During Reach to Grasp in the Monkey

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INTRODUCTION

When reaching to grasp an object, human and nonhuman primates characteristically preshape the hand to match object properties, such as size and shape (Castiello et al. 1993, 1998; Jeannerod 1984; Mason et al. 2004; Paulignan et al. 1991; Roy et al. 2002; Santello and Soechting 1998; Wing et al. 1986). A prominent view is that the necessary visuomotor or sensorimotor transformations required to shape the hand are mediated by parieto-frontal circuits involving the posterior parietal cortex, ventral premotor (PMv/area F5), and the primary motor cortex (M1) (Castiello and Begliomini 2008; Jeannerod et al. 1995; Raos et al. 2006; Rizzolatti et al. 1988). In this dorso-lateral circuit, object representations are hypothesized to be encoded in anterior intraparietal sulcus (AIP) in object-centered coordinates. In PMv these representations are hypothesized to be transformed into movement-based representations that are used to specify and control the specific grasp required.
The importance of M1 in prehension is further shown by the deleterious effects of lesions/inactivation of M1 (Brochier et al. 1999; Murata et al. 2008; Schieber and Poliakov 1998), the extensive activation observed during functional imaging (Ehrsson et al. 2000; Kuhtz-Buschbeck et al. 2008; Takasawa et al. 2003), and the alterations produced by transcranial magnetic stimulation (TMS) (Chouinard et al. 2005; Lemon et al. 1995; Schabrun et al. 2008). Furthermore, M1 neurons are highly active during both precision and power grasping (Gardner et al. 2007; Maier et al. 1993; Umilta et al. 2007; Wannier et al. 1991). The discharge of M1 neurons modulates in relation to multiple finger movements, the populations of neurons related to different fingers overlap extensively, and the projections from M1 diverge to multiple muscles (Poliakov and Schieber 1999; Rathelot and Strick 2006; Schieber 1991; Schieber and Hibbard 1993). These provide a neural substrate that could contribute to control of overall hand shape. M1 neurons have been shown to respond to properties of objects such as the texture and weight (Picard and Smith 1992) and the local field potentials in M1 vary with grasp configuration (Spinks et al. 2008), but the parameters of hand shaping represented by M1 neurons remains to be determined.

The discharge of M1 neurons also modulates with grasp force, although there are conflicting results on the degree of encoding of grasp force in the firing of PMd neurons during precision grip. Some studies found no correlation (Boudreau et al. 2001) and others found context-dependent correlations (Hepp-Reymond et al. 1999) between PMd firing rates and grasp force level. The discharge of M1 neurons modulates with the force during precision grip, although several studies have described inverse relationships (Hepp-Reymond 1988; Maier et al. 1993; Wannier et al. 1991). Functional imaging studies provide evidence that activation increases with grip force level (Dettmers et al. 1995; Ehrsson et al. 2002; Kuhtz-Buschbeck et al. 2008; Ward et al. 2008). During reach to grasp that included whole hand grasping, the discharge of M1 and PMd neurons modulate during application of grasp force (Gardner et al. 2007; Raos et al. 2004; Stark et al. 2007; Umilta et al. 2007). However, studies of the modulation of PMd and M1 neurons during whole hand grasp in an explicitly controlled task as well as varied grasp force are lacking.

This study investigated hand shaping and grasp force during whole hand prehension with three specific goals. The first goal was to investigate which specific parameters of object/hand shape are encoded in the firing of PMd and M1 neurons during reach to grasp. The second goal was to examine the contribution of whole hand grasp force to the firing of PMd and M1 neurons. The third goal was to assess the relationship between hand shaping and grasp force signals in neuronal firing. Behavioral studies support the hypothesis that these two aspects of prehension are controlled independently (Biegstraaten et al. 2006; Jackson and Shaw 2000; Mason et al. 2004, 2006). There is also some evidence for independent control in several regions in the CNS. For example, hand shape and grasp force signals are signaled relatively independently in the simple spike firing of Purkinje cells (Mason et al. 2006). A temporal dissociation in the control of hand shaping and grasp force has been identified in the AIP by TMS (Davare et al. 2007). Inactivation of F5 or AIP in the monkey results in deficits in hand preshaping while leaving grip force essentially intact (Fogassi et al. 2001; Gallese et al. 1994). Therefore the third goal assessed the degree to which these two parameters are independently present in the firing of PMd and M1 neurons.

To address these three goals, two rhesus monkeys were trained to reach to and grasp a set of objects with explicit grasp force requirements. Detailed kinematic analyses of the wrist, hand, and finger movements during the same task in the same animals have been previously published (Mason et al. 2004, 2006; Theverapperuma et al. 2005). The discharge of both PMd and M1 cells was predominantly related to properties of the object grasped with fewer neurons modulated by grasp force.

**Methods**

**Behavioral task**

The experimental protocol was approved and monitored by the University of Minnesota Institutional Animal Care and Use Committee and conformed to the “Guiding Principles in the Care and Use of Animals” of the American Physiological Society. The details of the behavioral paradigm and many of the experimental procedures were included in recent publications (Mason et al. 2004, 2006; Theverapperuma et al. 2005). Therefore only a brief description of these methods is provided in this report.

Two rhesus monkeys (monkey G: female, 5.2 kg; monkey L: male, 6.8 kg) were trained with their heads fixed to reach to and grasp objects at a specified grasp force level (Fig. 1A). Trials were initiated when the monkey placed its hand on a 5 × 5-cm start-pad located by the animal’s side. The monkey was required to maintain its hand on the start pad for a randomized period of 450–750 ms. A “go” cue (blue vertical bars), presented on a 15-in computer monitor at eye level, signaled the monkey to reach (~15 cm) and grasp the target object. The required grasp force range to be generated and maintained during the grasp was specified by the heights of two vertical bars. The left bar provided the lower and right bar the higher of the required force range. The monkeys were trained to grasp the objects with an overall moderate grasp while allowing considerable freedom in placing their fingers in contact with the force sensor to meet the force level requirements. Visual feedback of the applied force was provided by a vertically displaced red indicator bar. The monkeys received a juice reward if they successfully initiated (within a 0.5-s window) and maintained the specified grasp force level for 1.5 s.

This study examined the encoding of object properties in the absence of direct vision of the objects and hand. As described in our earlier study (Mason et al. 2004), the animals were highly trained and could recognize the unseen objects through touch. The animals were not allowed to see the target object or their hand but were allowed to touch objects before the initiation of each block of trials when objects were changed.

The 16 objects (Fig. 1B), mounted on a fixed metal shaft, were made of Lexan painted black and categorized within four geometric classes (cubes, rectangular prisms, poly-sided prisms, and cylinders). A Force Sensing Resistor (FSR 1.27 cm diam, Interlink Electronics, Camarillo, CA) was positioned on the face of each object opposite the monkey. Monkey G, which performed the task with the right hand only, was required to exert one of five instructed levels of anterior-posterior (AP) grasp forces on the object (0.2, 0.4, 0.6, 0.8, and 1.0 N, each level having an allowable target force range of ±0.1 N). On grasp initiation, the monkey was allowed a 500-ms window within which to acquire the target force level (e.g., reach target or correct for overshooting target force). As shown in Figs. 4 and 5, the animals rarely under or overshoot the desired grasp force. The monkey was required to maintain the target force level within the upper and lower tolerance range for 1.5 s before receiving a juice reward. Monkey L was trained to exert five force levels with its right hand but only three
of the five force levels (0.2, 0.6, and 1.0 ± 0.1 N) when performing the task with the left hand. Only three of the five force levels were used for the left hand to ensure the maximum number of objects (blocked trials) could be completed within a recording session. Objects were presented in random order with five repetitions for each of the force levels generated pseudorandomly within each block. For monkey L, object 1 (smallest cube) was not used for the right hand because the animal had difficulty mastering the grasp of this object at all five force levels. Behavioral data collected included the force generated on the target object as well as the time of the reach onset (i.e., time of lift-off from the start-pad) and grasp onset (i.e., time of the go cue). The details of the data collection from the monkey's hand touched the start-pad and ended with the presentation of the go-cue. The duration of the baseline epoch varied from trial to trial. The baseline epoch was defined as the 300 ms before movement onset, rather than the timing of the go cue, because the latter was not recorded in both animals. Reach onset was determined as the time the hand lifted from the start-pad force sensor (i.e., peak force deceleration less than −0.3 N). The reach epoch ended and initiation of the grasp epoch began when the force sensor on the target was first activated (object force sensor >0.1 N). The grasp epoch was limited to the initial 1,200 ms of grasp initiation and object hold.

All statistical analyses of firing were based on single trials, not averaged data, so that the data analyses accurately reflect the variability caused by the signal from that of the noise (Howell 2008) and to provide consistency with our study of Purkinje cell firing during this task (Mason et al. 2006). Averaging firing across trials will inflate $R^2$ values because the natural variation across trial repetitions (i.e., noise) is effectively aggregated within the estimate of the variability caused by the signal (Kenney 1979). Therefore the $R^2$ values reported in this study may appear smaller than studies using average firing, but the $R^2$ values must be understood in the context that all analyses were based on single trial data.

The first analysis of the firing was based on the task epochs. For each trial, four task-related epochs were identified (baseline, premovement, reach, and grasp). The baseline epoch began when the monkey's hand touched the start-pad and ended with the presentation of the go-cue. The duration of the baseline epoch varied from trial to trial. The premovement epoch was defined as the 300 ms before reach onset, rather than the timing of the go cue, because the latter was not recorded in both animals. Reach onset was determined as the time the hand lifted from the start-pad force sensor (i.e., peak force deceleration less than −0.3 N). The reach epoch ended and initiation of the grasp epoch began when the force sensor on the target was first activated (object force sensor >0.1 N). The grasp epoch was limited to the initial 1,200 ms of grasp initiation and object hold.

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The first analysis of the firing was based on the task epochs. To determine whether a cell was task related, a paired Student’s $t$-test evaluated whether the firing in the premovement, reach, and grasp
epochs was different from baseline firing (Mason et al. 2006). For cells defined as task related, an ANOVA was done on the mean firing rates during the premovement, reach and grasp epochs with object or object grasp dimension and with force level as treatment factors ($\alpha = 0.05$). As expected, grasp aperture, defined as the distance between the thumb and index finger, was found to vary linearly with the object grasp dimension (e.g., the grasp width of the object) (Mason et al. 2004). Grasp dimension provided a method of estimating one aspect of object shape as a single continuous variable.

Whereas the epoch-based ANOVA analysis provided evidence of significant differences in discharge across the independent variables, the post hoc analyses provided insight into the nature of this relationship (e.g., whether linear). The post hoc linear regression was based on the individual trial firing rates at each level of grasp dimension or grasp force. Replication across force levels and grasp dimension required use of a “lack-of-fit” test based on estimates of the deviations-from-linearity (Zar 1999). If the deviation from linearity was not significant ($P > 0.05$), the relationship between cell firing and force and grasp dimension was considered linear.

Temporal regression analysis

The epoch-based analysis was performed over relatively long duration periods. To provide a more precise measure of the timing of the cell correlation with either hand shape or grasp force, a bin by bin multiple regression analysis was computed (Fu et al. 1995, 1997; Mason et al. 2006). The temporal regression analysis was based on individual trials to insure high power statistical results (e.g., larger sample size) and a log transform of the firing was used so as to insure homogeneity of variance (Ashe and Georgopoulos 1994; Howell 1987). The firing, $F$, in each 16.67-ms bin ($t_i$) was regressed to the variables

$$F(t_i) = \beta_0(t_i) + \sum_{j=1}^{3} \beta_{force}(t_i)FORCE_j + \sum_{k=1}^{7} \beta_{gd}(t_i)GD_k \quad (I)$$

in which $FORCE$ is the grasp force level the monkeys needed to maintain during the task, and $GD$ represents the objects’ grasp dimension. The paradigm required that the monkey maintain the desired force level during the hold period or the trial was aborted. Therefore during the grasp epoch, the desired grasp force level and the actual grasp force exerted by the monkey were equivalent (Figs. 4 and 5, top row force plots). Total and partial (object grasp dimension and force) $R^2$ values were calculated using a multiple regression analysis (Edward 1979) for each object for the monkey $L$, $G$, and $C$ (monkey $L$ was trained on all 16 objects and used a precision grasp with the smallest cube. These studies also showed that reach kinematics remained constant across objects and grasp force levels, implying that modulation in the firing of the motor cortical cells was not related to variations in the reach. Hand shaping began with the initiation of reach and continued throughout the reach. Hand shape throughout the reach and grasp epochs was found to match object properties (e.g., size) but showed no significant relation to or interaction with the grasp force. For example, the shaping of the hand throughout the reach did not change with grasp force. Nor did arm kinematics vary with grasp force.

Task-related modulation and cell locations

The histology results indicated that cell recordings for both monkeys were generally located throughout the precentral gyrus, medial to the genu of the arcuate sulcus (Fig. 2). The classification of a cell as being within the PM (black) or M1 (gray) was based on the histology, and when available, ICMS results. The vast majority of the PM cells were located in the PMd where grasp-related neurons are located (Raos et al. 2004; Stark et al. 2007) and, therefore we will refer to the cell location as PMd.

Two hundred twelve PMd and M1 neurons were recorded in the two monkeys. A total of 170 cell recordings (35 for monkey $G$; 35 and 100 for monkey $L$, left and right chambers, respectively) were analyzed in this report, retaining only those neurons in which 4 or more of the 16 objects were successfully completed for five force levels (or 3 force levels for monkey $L$, left hand) and with at least five repetitions per treatment combination (e.g., a minimum of 60–100 trials per cell). The

**RESULTS**

**Behavior and kinematic analysis**

Analysis of the wrist, hand, and finger movements for this same task and monkeys was published previously (Mason et al. 2004, 2006; Theverapperuma et al. 2005). As detailed in the previous publications, monkey $G$ grasped objects 2–16 using a power grasp with a palm-finger opposition and used a precision grasp with the smallest cube (object 1). An analysis of precision versus power grip was therefore not possible because it would be based on insufficient data (i.e., the animals used a precision grasp with only 1 object). For the right hand, monkey $L$ used an overhand power grasp with a thumb-finger opposition for objects 2–16. For the left hand, monkey $L$ was trained on all 16 objects and used a precision grasp with the smallest cube. These studies also showed that reach kinematics remained constant across objects and grasp force levels, implying that modulation in the firing of the motor cortical cells was not related to variations in the reach. Hand shaping began with the initiation of reach and continued throughout the reach. Hand shape throughout the reach and grasp epochs was found to match object properties (e.g., size) but showed no significant relation to or interaction with the grasp force. For example, the shaping of the hand throughout the reach did not change with grasp force. Nor did arm kinematics vary with grasp force.

**FIG. 2.** A–C, cortical surface maps of reconstructed locations of microelectrode penetrations for the left motor cortical chamber in monkey $G$ (A) and the left (B) and right (C) in monkey $L$. Histology and intracortical microstimulation (ICMS) results were used to classify dorsal premotor cortex (PMd; black, $\geq$25 $\mu$A ICMS) and primary motor cortex (M1; gray, <25 $\mu$A ICMS) cell recording sites. ARC, arcuate; CENT, central; PRIN, principle.
The majority of the task-related cells responded primarily to propriocceptive manipulations (76%, PMd; 59% M1), with fewer cells having primarily cutaneous fields (24%, PMd; 41% M1). Most of the cells had receptive fields relating to the hand (48%, PMd; 82% M1), with fewer relating to the arm (24%, PMd; 14% M1) and/or shoulder areas (43%, PMd; 16% M1).

Task-related modulation was very common in the two cortical areas, including 91% (58/64) of the cells in PMd and 92% (98/106) of the cells in M1 (Fig. 3A). Significantly more M1 task-related cells were modulated during the reach (92%, 98/106) and grasp (84%, 89/106) epochs than during the premovement (71%, 75/106) epoch (χ² = 16.9, df = 2, P < 0.05). In contrast, the number of task-related PMd cells was constant across epochs (χ² = 1.7, df = 2, P > 0.05). The only difference in the task-related cells between the two areas was during the premovement epoch when significantly more PMd cells were modulated than M1 cells (χ² = 4.34, df = 1, P < 0.05). Mean firing rates also differed across epochs (Fig. 3B) with significantly higher firing rates during reach and grasp than during premovement (F(2,165) = 10.73 and 24.48, P < 0.05 for PMd and M1 cells, respectively). However, there was no difference in the average firing of task-related cells in PMd and M1 for the three epochs [F(1,424) = 0.93, P > 0.05]. In summary, PMd and M1 cells have similar firing rates across epochs and similar percentages of cells modulated during the behavioral epochs of reach and grasp. The only notable difference was that during the premovement epoch a greater percentage of PMd cells were task-related than in M1.

The firing patterns for two individual M1 cells are shown in Figs. 4 and 5. Each neuron was successfully isolated and discriminated for 15 objects at each of the five force levels with at least five repetitions for a total of ≥375 trials. Histograms of PMd and M1 firing were constructed to qualitatively assess the discharge modulation in relation to the task epochs, objects, and grasp force. Several aspects of the cell discharge modulations are shown by these examples. First, most PMd and M1 cells had significant modulation in their firing for more than one task epoch. Only a few cells had significant firing restricted to a single epoch (premovement: 2, reach: 11, or grasp: 2 cells). Cell L061 (Fig. 4), for example, showed significant differences in firing relative to baseline during premovement, reach, and grasp epochs [t(467) = 19.06, −52.53, and −52.90, respectively, P < 0.05]. Similarly, for cell L048, significant modulation occurred during each epoch [t(467) = −13.59, −67.25, and 29.64, respectively, P < 0.05], although the modulation in firing was predominantly related to reach (Fig. 5).

The second aspect of discharge modulation in PMd and M1 was that the temporal profiles were consistent across objects and grasp force. In cell L061 (Fig. 4), for which monkey L completed all objects except object 1, the firing rate increased during reach with peak firing just before or at the onset of grasp initiation. The firing slightly decreased in amplitude after grasp onset and was relatively sustained as the grasp force was held at target level. For cell L048 (Fig. 5), the temporal firing pattern consisted of an increase in firing followed by a decrease in firing during the reach epoch. The amplitude of the firing differed markedly for objects 6 and 13, yet the basic temporal pattern was preserved. A significant change in firing amplitude across objects was found during the premovement, reach, and grasp epochs [F(14,393) = 115.92, 14.58, and 12.37, respectively, P < 0.05]. Similar observations (i.e., relatively fixed modulation patterns that varied in amplitude with object) were noted for most PMd and M1 cells. Significant object-related firing was found for 149 (54/58 PMd and 95/98 M1) of the 156 task-related cells (ANOVA, P < 0.05).

The third property of the discharge was that some cells were modulated by grasp force. For example, there was an increase in firing with grasp force level (bottom-to-top histograms) during the reach and grasp epochs for cell L048 (Fig. 5; e.g., longer duration and increased firing with increased grasp force) but not during premovement. This increase was statistically significant [F(4,393) = 3.68 and 160.06, for reach and grasp epochs, respectively, P < 0.05; F(4,393) = 0.89, P > 0.05, for premovement epoch], but the overall effect size was small (R² = 0.015 for reach and R² = 0.024 for grasp epoch). A post hoc regression analysis confirmed that firing increased linearly with grasp force during both reach and grasp epochs (lack-of-fit test, P > 0.05). This example reflects the limited, yet significant, grasp force coding observed in the population (Fig. 8D). Examples of more robust encoding of grasp force can be seen in Figs. 7E and 10E. However, cell L061 (Fig. 4) showed no significant modulation with grasp force during any of the epochs [F(4,438) = 0.64, 0.13, and 0.44, for premovement, reach, and grasp, respectively, P > 0.05]. These findings warranted a more detailed analysis of cell discharge as a function of object properties and grasp force levels across epochs.
Modulation with grasp dimension and grasp force

As described above, PMd and M1 cells were significantly modulated by object. Given the importance of grasp aperture in prehension, we examined the relation between cell firing and grasp dimension. An example of a PMd neuron with significant differences in firing across object grasp dimension is shown in Fig. 6, A–D. The grasp dimension was a significant factor for premovement, reach, and grasp epochs \( F(6,249) = 15.79, 26.10, \) and 15.07, respectively, \( P < 0.05 \). A post hoc analysis showed that firing was not linearly related to object grasp dimension during the premovement, reach, and grasp epochs \( [\text{lack-of-fit test, } F(5,263) = 13.68, 18.04, \text{ and } 10.09, \text{ respectively, } P < 0.05] \). suggestive of a more complex relation between firing and grasp dimension. For this cell, there was no significant difference in the firing as a function of the grasp force level for any of the epochs \( F(2,249) = 0.26, 0.39, \text{ and } 1.03, \text{ respectively, } P > 0.05 \). An M1 cell with significant differences in the mean firing rate as a function of object grasp dimension is shown in Fig. 7. Significant differences in the firing rate was noted across object grasp dimension for each epoch \( F(5,243) = 2.52, 30.00, \text{ and } 24.00, \text{ respectively, } P < 0.05; \text{ Fig. 7, B–D} \). The relation between firing and object grasp dimension was not linear \( [\text{lack-of-fit test, } F(4,462) = 3.2, 36.12, \text{ and } 25.85 \text{ for premovement, reach, and grasp, respectively, } P < 0.05] \). A significant force effect was found during the grasp epoch \( F(4,438) = 15.97, P < 0.05 \), and a post hoc regression indicated that firing rates increase linearly with the grasp force level \( [\text{lack-of-fit test, } F(3,463) = 0.43, P > 0.05; \text{ Fig. 7H}] \). No significant force-related effects were noted during the premovement and reach epochs \( F(4,438) = 0.26 \text{ and } 0.81, P > 0.05; \text{ Fig. 7, F and G} \). There was no significant interaction between object grasp dimension and grasp force \( P > 0.05 \).

For the population of cells, most PMd (93%, 53/58) and M1 (97%, 95/98) task-related cells were significantly modulated by grasp dimension during at least one epoch (Fig. 8A). Almost all task-related cells with object grasp dimension signaling (117/156) were modulated during at least two or more epochs. Overall, the correlation of the firing with grasp dimension was greater for M1 neurons. Across epochs, the percentage of cells

[FIG. 5. Example of a task-related M1 cell (L048) with significant object- and force-related firing. Conventions as in Fig. 4.]

[FIG. 4. Example of a task-related M1 cell (L061) with significant object-related firing. Histograms and force profiles represent the averaged cell firing rate and grasp force levels, respectively, across all trial repetitions for each object (2–16) and force level (1–5 N). Histograms are ordered with the repetitions of the lowest force (0.2 N) on the bottom and highest force (1.0 N) on the top for each object. In this and subsequent figures, all data were aligned on grasp initiation (time = 0). Three vertical dashed lines represent the average onset times for the premovement (P), reach, and grasp epochs.]

Significant differences in the firing rate was noted across object grasp dimension for each epoch \( F(5,243) = 2.52, 30.00, \text{ and } 24.00, \text{ respectively, } P < 0.05; \text{ Fig. 7, B–D} \). The relation between firing and object grasp dimension was not linear \( [\text{lack-of-fit test, } F(4,462) = 3.2, 36.12, \text{ and } 25.85 \text{ for premovement, reach, and grasp, respectively, } P < 0.05] \). A significant force effect was found during the grasp epoch \( F(4,438) = 15.97, P < 0.05 \), and a post hoc regression indicated that firing rates increase linearly with the grasp force level \( [\text{lack-of-fit test, } F(3,463) = 0.43, P > 0.05; \text{ Fig. 7H}] \). No significant force-related effects were noted during the premovement and reach epochs \( F(4,438) = 0.26 \text{ and } 0.81, P > 0.05; \text{ Fig. 7, F and G} \). There was no significant interaction between object grasp dimension and grasp force \( P > 0.05 \).
with significant modulation with grasp dimension (Fig. 8A), and the average $R^2$'s for the fit (Fig. 8B) were greater for M1 than PMd [percentage, $\chi^2 = 20.76$, df = 1, $P < 0.05$; $R^2$ grasp dimension $F(1,311) = 9.03$, $P < 0.05$]. For PMd and M1, the percentage of cells with significant modulation with grasp dimension increased as reach to grasp progressed from premovement (41%, 24/58 and 58%, 57/98) to reach (59%, 34/58 and 84%, 82/98) and grasp (60%, 35/58 and 85%, 83/98; $\chi^2 = 24.4$, $P > 0.05$). The average $R^2$'s for grasp dimension differed across epochs [$F(2,311) = 8.88$, $P < 0.05$], with the $R^2$'s significantly increasing from the premovement to the reach and grasp epochs (post hoc Bonferroni adjusted, $P < 0.017$), and this was consistent across PMd and M1 cells [i.e., no interaction effect $F(2,311) = 0.20$, $P > 0.05$]. Finally, post hoc linear regressions testing for "lack-of-fit" showed that a modest fraction of the cells modulated with object grasp dimension had firing rates linearly related to grasp dimension during the premovement (PMd: 33%, 8/24; M1: 25%, 14/57), reach (PMd: 6%, 2/34; M1: 16%, 13/82), and grasp (PMd: 20%, 7/35; M1: 12%, 10/83) epochs.

A second analysis assessed whether other measures, categorical or continuous, provided additional or better information compared with object grasp dimension. Therefore in addition to object grasp dimension, the firing was modeled with object volume and object class in separate regressions (ANOVA, $\alpha = 0.05$). When comparing object grasp dimension, object volume, and object class, the percentage of significantly modulated cells was 53 (31/58), 52 (30/58), and 44% (26/58) for PMd and 75 (74/98), 75 (73/98), and 67% (65/98) for M1, respectively (based on the average over the 3 epochs). Although there were significant differences in the fraction of cells modulated by these three properties ($\chi^2 = 9.78$, df = 2, $P < 0.05$), this is not unexpected because the firing of a much smaller number of cells was modulated in relation to object class than grasp dimension or object volume (pairwise contrasts, class and grasp dimension, $\chi^2 = 9.70$, df = 1, $P < 0.05$; class and volume, $\chi^2 = 3.23$, df = 1, $P < 0.05$; grasp dimension vs. volume, $\chi^2 = 1.6$, df = 1, $P > 0.05$). Most important was the almost complete overlap of the cells significantly modulated by object grasp dimension and volume (95% of

**FIG. 6.** A and B: example of a PMd cell (L553) with object grasp dimension related modulation. Color plots for the mean firing rate by object grasp dimension (A) and grasp force (E). B–H: mean firing rates and SE across object grasp dimension (B–D) and force level (F–H) during the premovement (B and F), reach (C and G), and grasp epochs (D and H). Post hoc linear regressions indicated that cell firing was not linearly related to object grasp dimension during the 3 epochs. Vertical lines above the color plots represent the average onset times for the premovement, reach, and grasp epochs with the SD of reach onset indicated by a horizontal bar at the top.

**FIG. 7.** A and B: example of an M1 cell (L052) with object grasp dimension and force-related modulation. Color plots for the mean firing rate by object grasp dimension (A) and grasp force levels (E). B–H: mean firing rates and SE across object grasp dimension (left) and force level (right) during the premovement (B and F), reach (C and G), and grasp (D and H). Post hoc linear regressions indicated that cell firing was not linearly related to the object grasp dimension. Cell firing was linearly related to grasp force during the grasp epoch. Conventions as in Fig. 6.
the cells modulated by grasp dimension were also modulated by object volume). Similarly, there was also a nearly complete overlap for cells modulated by object grasp dimension and class (95%) and object volume and class (94%). Therefore the analysis based on object volume or class did not provide additional information on the parameters of object shape represented in these neurons.

Only a minority of PMd (33%, 19/58) and M1 (40%, 39/98) task-related cells modulated with grasp force (Fig. 8C). Significantly more cells were modulated in response to grasp dimension than grasp force for both cortical areas (PMd, χ² = 57, df = 1, P < 0.05; M1, χ² = 180, df = 1, P < 0.05). More cells with force-related modulation were recruited during the grasp epoch compared with premovement and reach epochs (χ² = 32.09, df = 2, P < 0.05) when force was actually applied to the object. Of the 19 PMd cells with force-related modulation, 14 of these cells modulated with force during the grasp epoch. Of the 39 M1 cells with force related modulation, 32 of these cells modulated with force during the grasp epoch. No differences in cell percentages were noted between PMd and M1 cells across epochs (χ² = 0.06, df = 1, P > 0.05) or within epochs (χ² = 1.17, df = 2, P > 0.05, no interaction effect). However, the average R² for the fit to grasp force did not differ across epochs [F(2,61) = 1, P > 0.05] or for PMd and M1 cells [F(1,61) = 0.01, P > 0.05; Fig. 8D]. Cells with grasp force modulation had predominantly linearly related firing with grasp force during premovement (PMd: 60%, 3/5; M1: 67%, 4/6), reach (PMd: 67%, 2/3; M1: 86%, 6/7), and grasp (PMd: 100%, 14/14; M1: 84%, 27/32). All cells with significant force-related modulation also had a significant grasp dimension effect. However, only a few cells (1/53 PMd and 8/95 M1) had a significant grasp dimension by force interaction effect. The interaction effect was primarily observed during the grasp epoch (PMd 1/1 and M1 7/8).

The linear regression analysis showed that a smaller fraction of PMd and M1 cells were significantly modulated by grasp force than grasp dimension. It is possible that the lower recruitment levels and smaller R²s observed for grasp force may be compensated by larger modulation levels in the firing rate such that the effect size was greater. To examine this possibility, effect size was defined as the percent change in the mean firing rate between lowest and highest factorial levels (i.e., difference between grasp dimensions or grasp force levels with the lowest and highest mean firing rates). Overall, the percent change in firing was greater for grasp dimension than force-related modulation [F(1,261) = 53.32 and F(1,109) = 7.93, P < 0.05; grasp dimension 54 ± 20 and 48 ± 18; force 31 ± 17 and 33 ± 13 spikes/s for PMd and M1, respectively]. No differences were noted across epochs [F(2,261) = 5.63, P < 0.05 but no significant post hoc Bonferroni multiple comparison, and F(2,109) = 0.90, P > 0.05; premovement 49 ± 21 and 43 ± 18; reach 48 ± 21 and 46 ± 18; grasp 52 ± 22 and 46 ± 18 spikes/s for PMd and M1 cells, respectively] or cell types [F(1,1370) = 0.30, P > 0.05; PMd 50 ± 21 and M1 45 ± 18 spikes/s]. Therefore for the three measures examined (percent cells with significant modulation, model R², and effect size), cell firing was more strongly correlated with grasp dimension than grasp force.

Timing of the grasp dimension and grasp force modulations

The epoch-based analyses showed that PMd and M1 cell discharge modulated in relation to object grasp dimension and grasp force. However, the firing histograms indicated that the cell firing changed within epochs as well as during the transitions between epochs (Figs. 4 and 5). Furthermore, brief periods of cell modulation could be masked by averaging the firing rate over the entire grasp segment (1,200 ms). Therefore a linear multiple regression model (Eq. 1) relating cell firing to grasp dimension and grasp force over time was used to more precisely define the timing of the modulations.

An example of the temporal regression analysis for a PMd cell is shown in Fig. 9. The R²model (Fig. 9A) as a function of time was significant for most time bins (top raster plot, P < 0.05) during the reach and grasp epochs but not during the premovement epoch. The R²model increased during the reach, attaining peak amplitude mid-reach. A secondary peak in R²model occurred during grasp initiation followed by a brief segment of nonsignificant R²model ~300 ms after grasp initiation. The R²model was again significant during the remainder of the grasp epoch. Examination of the model’s partial R² for object grasp dimension, R²gd (Fig. 9B) and grasp force level, R²force (Fig. 9C) indicated that most of R²model was related to the object grasp dimension rather than the grasp force level. The difference was further exemplified by the color plots of the mean firing rates over time for grasp dimension and grasp force–related firing (Fig. 9, D and E, respectively). Firing increased monotonically and linearly with increased grasp force levels [F(4,438) = 2.50, P < 0.05, post hoc lack-of-fit test, F(3,463) = 0.82, P > 0.05; Fig. 9E], although the overall change in firing was small. In contrast, firing showed greater differences in both onset and magnitude across object grasp dimension (Fig. 9D).

An example of the temporal regression analysis for an M1 cell is shown in Fig. 10. The R²model (Fig. 10A) as a function of time was significant for some of the premovement epochs and most of the reach and grasp epochs (top raster plot, P < 0.05). The R²model had relative peaks during the premovement, at the end of the reach, and during the grasp force hold. A closer examination of R²gd (Fig. 10B) and grasp force level, R²force (Fig. 10C) indicated that most of R²model was related to the object
grasp dimension during the premovement and reach epochs but largely related to the force during the grasp epoch. Firing decreased linearly with grasp force \([F(2249)=31.52, P<0.05, \text{post hoc lack-of-fit test}, F(1267)=1.53, P>0.05, \text{Fig. 10E}]\).

Across the PMd and M1 cell populations, the firing of more M1 (gray) than PMd (black) cells had significant \(R^2\) model and \(R^2\) gd (Fig. 11, A and B) during all three epochs. A greater fraction of M1 cells had a significant \(R^2\) force for all epochs compared with PMd cells and this difference was most pronounced during grasp (Fig. 11 C). The mean grasp \(R^2\) force exhibited a similar trend (Fig. 11 F). The model and grasp dimension \(R^2\) s for M1 cells increased throughout reach, peaking at grasp onset, and remaining relatively high during the grasp epoch (Fig. 11, D and E). The model and grasp dimension mean \(R^2\) s for PMd cells also increased during reach and then plateau, but the increase was much less pronounced than observed for M1 cells.

**DISCUSSION**

**Firing modulation in PMd and M1 with grasp dimension**

The first major finding of this study is that both PMd and M1 cells are significantly modulated by grasp dimension. As described in previous studies, a large percentage of task-related neurons in PMd (93%) and M1 (97%) modulate in relation to the object grasped (Raos et al. 2004; Stark et al. 2007). This study extends those findings by showing that a specific parameter of hand shape, grasp dimension, is signaled in the firing of PMd and M1 neurons. This modulation occurred during the premovement, reach, and grasp epochs, consistent with a role for PMd and M1 in both the planning and execution of hand shape.

The control of grip aperture is a critical parameter of prehension. Grip aperture increases during the first half of reach, followed by gradual closure of the grip to match the object (Castiello et al. 1998; Jeannerod 1981, 1984; Paulignan et al. 1991; Santello and Soechting 1997, 1998). For both PMd and M1, there was an increase in the modulation of firing with grasp dimension as the task evolved that was evident in both the epoch-based (percentage of cells modulated, \(R^2\), and effect size) and temporal regression analyses. We hypothesize that this temporal progression reflects the matching of the grip aperture to the grasp dimension that occurs during the second half of the reach and during the grasp period.

The modulation with grasp dimension was more prevalent in M1 than PMd neurons. This suggests that grasp dimension is strongly represented in the final stages of motor cortical processing of hand shape. Intrinsic hand muscles receive the
strongest cortical input just before contact, as fingers close around the object, and at grasp initiation just as contact with the object is achieved (Lemon et al. 1995). Similarly, peak grasp dimension encoding (temporal $R^2$) occurred shortly before and just after the transition from reach to grasp epochs in M1 and, to a lesser extent, in PMd. These findings are consistent with the hypothesis that a critical transition from reach to grasp-related processing occurs within M1 during the late-reach phase of reach to grasp (Lemon et al. 1995).

Parameters of hand shape (or their correlates) in addition to grasp dimension are likely to be represented in the firing of PMd and M1 neurons. The activity of PMd neurons is modulated during grasping and exhibit preference for different grips (Raos et al. 2004; Stark et al. 2007). Similarly, PMv neurons encode goal-related hand motor behaviors such as grasping and manipulating objects as opposed to movements of single digits (Murata et al. 1997; Raos et al. 2006; Rizzolatti et al. 1988). However, our analysis of other possible parameters of hand shape, including object volume and shape, did not provide any additional insights into what those parameters may be. Other object factors known to influence hand shaping and grasp such as fragility, texture, and weight have been studied (Savelsbergh et al. 1996; Weir et al. 1991a,b).

Whether there are underlying parameters of motor control that produce the strong correlation between the firing of PMd and M1 neurons and object properties is a critical question. Not only does hand shape change with the different objects, but so do patterns of muscle activation (Brochier et al. 2004). These patterns of muscle activation change in time during reach to grasp, not unlike the firing properties of PMd and M1 neurons in this study. Specifically, the transition from reach to grasp in the firing might be related to muscles involved with extending and then abducting the fingers, such as the extensor digitorum communis (Brochier et al. 2004). However, although this study was not designed to dissociate kinematic versus muscle activity, it is unlikely that these cells purely encode muscle activity given the limited grasp force-related effects. Another likely candidate is the kinematics of the individual fingers because movements of the fingers highly modulate cells widely distributed in M1 (Hamed et al. 2007; Poliakov and Schieber 1999; Schieber 2002; Schieber and Poliakov 1998). Elucidating the degree to which finger kinematics explain the correlations with object properties will require a study in which the movements of individual digits are monitored during reach to grasp.

The modulation of firing with object properties and hand shape were not due to visual inputs because the animals did not have vision of their hand or objects during reach-to-grasp. The animals did have a priori knowledge of which object was being presented (Mason et al. 2004). Also, during the initial training, monkeys were allowed to use visually guided reach to complete the task. This was sufficient for the monkeys to achieve the appropriate shaping of the hand without vision of the hand or object (Mason et al. 2004). Furthermore, hand shaping synergies in the monkey do not rely on vision (Mason et al. 2004). This is consistent with human subjects, because the removal of continuous vision of the hand or object has little effect on hand preshaping during reach (Santello 2002; Santello et al. 2002; Schettino et al. 2003; Winges et al. 2003). Furthermore, grasp neurons in both PMv and PMd maintain object-related encoding during reach to grasp, regardless of the presence or absence of visual feedback (Raos et al. 2004, 2006). Therefore much of the evolution of the hand shape during reach to grasp can be achieved via feedforward control and/or proprioceptive/tactile feedback.

**Firing modulation with grasp force**

The second major finding is that the firing of only a fraction of PMd and M1 cells was modulated by grasp force, and this was largely during the grasp epoch when force was actively applied to the object. During the premovement and reach epochs, grasp force was significantly modulated in only a small fraction of the cells in either area. A larger fraction of the cells were modulated (~26% in PMd and ~34% in M1) during grasp, but the overall effect size remained smaller than for grasp dimension. The fraction of PMd cells responsive to force magnitude during the grasp is similar to that found in other premotor areas in response to predictable force/pulse perturbations during a precision grasp including ~33% in PMd, 28% in the supplementary motor area (SMA), and 38% in the ventral cingulate motor area (CMAv) (Boudreau et al. 2001; Cadoret and Smith 1997). However, the fraction of M1 cells was considerably...
lower than previously found for precision grasp (61% in caudal zone and 54% in rostral zone) (Boudreau and Smith 2001; Picard and Smith 1992) or during precision step-tracking/ramp-hold grasp (50–62% in premotor and motor areas) (Hepp-Reymond et al. 1994, 1999; Maier et al. 1993).

The relatively limited grasp force modulation in M1 neurons may be somewhat surprising. One possibility is that this small fraction of cells encoding grasp force could have a disproportionate influence. However, firing rates and depth of modulation as a function of grasp force were not disproportionately large or different. Another factor is that modulation of M1 neurons with force is not a simple proportional linear relation. For example, in M1 the best modulation can occur at smaller grip forces (Evarts et al. 1983; Hepp-Reymond et al. 1978), and an inverse relation between grip force and firing has been commonly reported (Hepp-Reymond 1988; Maier et al. 1993; Wannier et al. 1991). Other studies emphasized the encoding of dynamic aspects of precision grasp force in M1 (Boudreau and Smith 2001; Hepp-Reymond et al. 1999; Picard and Smith 1992). However, this study found that the firing correlations with static, whole hand, grasp force over a wide range were present in a minority of cells and the average effect size was small.

Recent TMS studies question a primary role for M1 in specifying and generating grip force. TMS of M1 does not result in marked disruption of grasp force. The major effect of applying TMS during reach to grasp was to delay the onset of load force from the time of initial digit contact (Lemon et al. 1995). The overall profiles of the grasp and load forces were only minimally altered. Virtual lesions of M1 induced by TMS do not alter the preload duration, maximal grip force, the overall grip force profile, or the ability to execute the grasp task (Chouinard et al. 2005; Schabrun et al. 2008). The main effects of virtual lesions include a 40-ms lag in the grip force relative to the grasp force and the loss of force scaling based on information obtained from previous trials. Therefore M1 does not seem essential to the specification of grasp force, consistent with the limited force signaling observed in the neural firing.

For PMd, the relatively low percentage of cells modulated by grasp force and the corresponding modest R² values are not unexpected. Studies of force coding in the firing of PMd neurons during arm or wrist movements show that limb kinematics are poorly represented (Xiao et al. 2006). Recent TMS studies in humans provide further evidence that PMd is unlikely a major contributor to the specification of grasp (load) force (Chouinard et al. 2005; Davare et al. 2006). Similarly, PMv is an unlikely site because inactivation in the monkey and human introduces deficits in hand preshaping (Gallese et al. 1994) while leaving grip force adjustments intact (Davare et al. 2006; Fogassi et al. 2001).

The small numbers of PMd and M1 cells involved in the encoding of grasp force raises the question of how and where the grasp force is specified in the motor system. One possible explanation is that the recording locations in this study were relatively anterior in M1 and not in the bank of the central sulcus (Fig. 2). Force-related modulation during limb tasks is more prominent in posterior M1, particularly in the bank of the central sulcus (Kalaska and Hyde 1985; Kalaska et al. 1989; Sergio et al. 2005), and recordings in this region may uncover stronger encoding of grasp force. Human functional imaging studies report positive relationships between activation and grip-force magnitude in M1 or M1/S1 (Dettmers et al. 1995; Ehrsson et al. 2002; Kuhtz-Buschbeck et al. 2008; Thickbroom et al. 1998; Ward et al. 2008). Imaging studies also suggest that the control of grip forces is widely distributed in the CNS including not only frontal and cingulate motor cortical areas but also regions in the parietal, frontal, and occipital cortex as well as in the thalamus, basal ganglia, and cerebellum (Bursztyń et al. 2006; Kuhtz-Buschbeck et al. 2008; Vaillancourt et al. 2003). However, the cerebellum is an unlikely site because previous findings from the same monkeys showed limited specificity for grasp force in the simple spike firing of Purkinje cells (Johnson and Ebner 2000). Furthermore, limb kinematics has little influence on the discharge of Purkinje cells during arm movements (Pasalar et al. 2006). Therefore the structures or networks responsible for the generation and scaling of grasp forces remains to be determined.

The monkey controlled the grasp force using visual feedback. This type of feedback is not representative of natural prehensile activity. Controlling grasp force using visual feedback engages a more widely distributed network of cortical and subcortical regions than does internally guided force control from memory (Vaillancourt et al. 2003). The increase in the number of PMd and M1 cells with force modulation during the grasp epoch, when the visual feedback was provided, may be the result of the engagement of this larger and more distributed network.

**Relationship of PMd to M1**

Whether looking at task (e.g., firing relative to baseline) or specific parameters (e.g., grasp dimension and grasp force), the firing of PMd and M1 neurons show similar properties. This includes the dominant encoding of grasp dimension over grasp force. Furthermore, the temporal profile of the grasp dimension signals, although less pronounced in PMd, largely mirrored that of M1. Encoding of similar parameters would provide for an efficient information exchange between PMd and M1. The similarity in encoding of grasp-related information in PMd and M1 confirms functional MRI (fMRI) results in humans (Begliomini et al. 2007) and is consistent with the concept that PMd controls grasp, at least in part, through its direct connections with the M1 (Castaillo and Begliomini 2008; Raos et al. 2004).

**Independent control of hand shaping kinematics and grasp force**

Individual PMd and M1 neurons signal both object properties and grasp force. These signals are encoded largely independently, that is a change in cell modulation related to grasp force has no relation to a change in modulation related to object grasp dimension. The encoding of multiple parameters in the firing of individual neurons is common in the CNS, including motor systems (Johnson and Ebner 2000; Johnson et al. 2001). However, different structures use different methods to signal and combine motor parameters such as direction, speed, and position. The seemingly ambiguous encoding of direction, speed and amplitude in PMd and M1 neurons during arm movements is resolved using a temporal parcellation scheme in which parameters are encoded at different times during movements (Fu et al. 1995; Johnson and Ebner 2000). In contrast, Purkinje cells of the cerebellum signal similar parameters simultaneously, presumably allowing the motor system to derive an aggregate parameter, such
as velocity (Fu et al. 1997; Johnson and Ebner 2000; Roitman et al. 2005). The strategy for signaling grasp dimension and grasp force for PMd and M1 neurons described here is the same as found for cerebellar Purkinje cells in the same task (Mason et al. 2006). What is not clear is whether these signals are combined to represent an aggregate parameter of grasping and if so, where in the CNS this combination occurs (e.g., downstream of PMd and M1). One view would be to keep these signals separate as suggested by the behavioral evidence (Biegstraaten et al. 2006; Jackson and Shaw 2000; Mason et al. 2004, 2006). Maintaining separate processing and control of grasp kinematics and kinetics would allow for the accommodation of a large repertoire of prehensile behaviors.

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