The Cortical Control of Visually Guided Grasping

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People have always been fascinated by the exquisite precision and flexibility of the human hand. When hand meets object, we confront the overlapping worlds of sensorimotor and cognitive functions. The complex apparatus of the human hand is used to reach for objects, grasp and lift them, manipulate them, and use them to act on other objects. This review examines what is known about the control of the hand by the cerebral cortex. It compares and summarizes results from behavioral neuroscience, electrophysiology, and neuroimaging to provide a detailed description of the neural circuits that facilitate the formation of grip patterns in human and nonhuman primates. NEUROSCIENTIST 14(2):157–170, 2008. DOI: 10.1177/1073858407312080

KEY WORDS Reach-to-grasp, Functional imaging, Parietal cortex, Frontal cortex, Primary motor cortex, Transcranial magnetic stimulation

Man has always been fascinated by the hand and the brain that steers it. Aristotle was one of the earliest to record his admiration for the versatility of the human hand. “The hand can become a claw, a fist, a horn or spear or sword or any other weapon or tool. It can be everything because it has the ability to grasp anything or hold anything.” The highly developed ability of the hand to grasp and manipulate objects under precise visual control is one of the key features of the human motor system. The skilled use of the hand is fundamental to the technological, social, and cultural progress of the human species (Lemon 1993; Tallis 2004).

In recent years, there have been significant advances in our understanding of the neural mechanisms underlying the transformation of visual information about an object in the outside world into motor commands that allow the hand to be shaped for efficient grasp of the object. The huge variation in the shape, size, and texture of the objects we must daily interact with in a skillful and precise manner demands that this transformation provide a highly specific and selective matching of the object’s properties to the motor commands for grasp and manipulation.

The complex neural architecture of the hand poses challenging questions for understanding the neural control that underlies the coordination of finger movements required for a wide variety of grasping tasks. Hence, a number of experimental approaches, from studies of hand kinematics to functional imaging, and cortical activities have been used to extend our knowledge of neural control of the hand.

Herein we review what is known about the control of the hand by the cerebral cortex and make parallels between studies in humans and macaque monkeys. This control must be exerted through a number of neural mechanisms, some of which are concerned with the deployment of individual finger movements, and others that involve a specialized visuomotor system that encodes object features and generates the corresponding hand configurations.

In the first section, we briefly define some of the methods and procedures used to study neural mechanisms related to grasping in humans and macaques. The ensuing sections summarize results from electrophysiological, neuroimaging, and lesion studies that have identified specific regions involved in the visuomotor transformation processes underlying grasping in monkeys and humans. The final section addresses possible developments for the further understanding of the cortical networks involved in grasping.

Methods for Studying Grasping Networks in the Brain

The majority of studies examined in this review utilized neurophysiological techniques such as single-cell recordings and neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). Among these techniques, single-cell recording has the highest resolution and provides much information about the activities of a few neurons in time. PET and fMRI detect variations in blood flow properties as a consequence of increases or decreases in neuronal activity (Fox and Raichle 1986; Bandettini and others 1993; Logothetis and others 2001). Another technique used to study brain functions related to grasping is transcranial magnetic stimulation (TMS), which can be used to temporarily disrupt or stimulate the cortex in a localized region (Pascual-Leone and others 2000).
Ideally, one might want to use the above techniques to study the brain of a monkey or a person who is performing a similar real-world grasping task that allows a comparison across experiments and species. This is an important aspect to be considered given that researchers have often presumed that the human brain contains homologues of areas in the macaque brain that are involved in grasping. In this respect, a potential problem emerges when inspecting the paradigms utilized in monkey and human grasping studies. Some studies consider non-visually-guided isometric grip tasks that mainly concern force measurements. Other studies consider the posture assumed by the hand in contact with the object as a result of a visually guided process. This process first involves a progressive opening of the grip with straightening of the fingers during reaching, followed by a closure of the grip until it matches object size and shape. Here we shall consider only studies of the latter type. This choice was dictated by the fact that in recent years neurophysiologists have made an effort to record neuronal activity from key areas using very similar paradigms in terms of reach-to-grasp tasks and stimuli (Fig. 1A-B). Furthermore, a number of functional neuroimaging, TMS, and lesion studies on humans have utilized a similar approach (Fig. 1C-D).

**Visuomotor Transformations for Grasping**

*Macaque Neurophysiological Research*

An important step forward in understanding how the brain controls grasp was the identification of a “visuomotor grasping circuit” (Jeannerod and others 1995; Fagg and Arbib 1998; Rizzolatti and Luppino 2001). This model proposes that the representations of visual and other sensory properties of external objects are stored within a specific sector of the posterior parietal cortex, namely, the anterior intraparietal sulcus (AIP; Taira and others 1990; Murata and others 1997, 2000). The general agreement is that the processes occurring in AIP constitute the initial step of the transformation leading from representation of objects to movement (Taira and others 1990; Sakata and others 1995; Murata and others 2000). AIP neurons fall into 3 main classes: “motor dominant,” “visual and motor,” and “visual-dominant” neurons. Motor-dominant neurons discharge during grasping and holding movements in both light and dark, but they are silent during object fixation. Visual-dominant neurons discharge during grasping in light and object fixation, but not during grasping in the dark. Visual and motor neurons discharge stronger during grasping in light than in dark. In addition, they discharge during object fixation. The fact that they respond more vividly during grasping in light signifies a more potent response dictated by the vision of the object. Furthermore, in most visual and motor neurons, the visually effective object and type of grip coded coincided. In this respect, other studies have revealed shape-specific responses in AIP during spontaneous grasp of random objects such as fruits, rulers, blocks, and geometrical shapes (Iwamura and Tanaka 1978; Iwamura and others 1985, 1995; Gardner and others 2002, 2007).

The demonstration that AIP is crucial for grasping comes from transient inactivation of AIP by injecting a GABA-receptor agonist (muscimol) (Gallesse and others 1994). Following AIP inactivation, there was a clear impairment of the grasping behavior of the hand contralateral to the inactivated hemisphere. The deficit consisted in a mismatch between the intrinsic properties of the object (e.g., size and shape) to be grasped and the hand shaping necessary to grasp it. The consequence was awkward object grasping or even a complete grasping failure. Among the various types of grip, that most impaired was the precision grip. Altogether these results...
support the view that the parietal neurons involved in manipulation play a specific role in the visuomotor transformation that is used for grasping objects.

**Ventral Premotor Cortex (Area F5)**

Single-neuron recordings performed using the same approach used for studying AIP neurons (Fig. 1A) showed that the firing of the majority of neurons of area F5, which is located in the posterior bank of the inferior limb of the arcuate sulcus and the cortical convexity immediately adjacent to it (Matelli and Luppino 1996; Rizzolatti and others 1998), was correlated with specific goal-related distal motor acts and not with single movements (Rizzolatti and others 1988). Execution of distal motor acts such as grasping,
holding, manipulating, and tearing is very effective in triggering F5 neuron responses. Interestingly, many hand-grasping neurons also show specificity for the type of prehension that is performed to grasp an object. Among these different types of grasp, precision grip (PG), characterized by the opposition of the thumb to the index finger, is the most represented type. Furthermore, there is specificity for different finger configurations, even within the same grip type (Rizzolatti and others 1988).

On the basis of this evidence, it has been proposed that in area F5 there is a “vocabulary” of elementary motor acts in which each “word” corresponds to a category of motor neurons that represents either the goal of the action or the way in which an action is executed, or the temporal segmentation of the action (Rizzolatti and others 1988). Very often there is a strict relationship between the type of prehension coded by a neuron and the physical characteristics of the stimulus effective in triggering its visual response (Rizzolatti and others 1988). Inactivation of F5 (Fogassi and others 1988) by injecting muscimol produced visuomotor deficits similar to those observed following AIP inactivation (Gallese and others 1994).

**Dorsal Premotor Cortex (Area F2)**

Area F2 (Matelli and others 1991; see also Matelli and others 1985) occupies the caudal two thirds of superior area 6 (PMd). It is located anterior to area M1, extends rostrally approximately 3 mm in front of the genu of the arcuate sulcus, and, laterally, up to the spur of the arcuate sulcus, which separates it from inferior area 6 (Fig. 2).

A number of studies have demonstrated that the discharge of the dorsal premotor neurons is correlated to parameters of reaching movements such as direction and amplitude (Caminiti and others 1991; Kalaska and others 1997; Wise and others 1997). In these studies, however, only proximal forelimb movements were taken into account; the contribution of the distal forelimb movements to the neuronal discharge has not been considered until recently. Raos and others (2004) demonstrated that within area F2 a distal forelimb field also exists. This study provides compelling evidence that in the distal forelimb representation of area F2, there are neurons that are selective for the type of prehension required for grasping the object. The activity of these grasping neurons was not related to individual finger movements but to the grasping action as a whole. Specifically, the proposal here is that area F2 has the role of keeping in memory the motor representation of the object and combining it with visual information as to continuously update the configuration and orientation of the hand as it approaches the object to be grasped. In this view, the PMd involvement during goal-directed actions appears to be highly correlated with the accuracy requirement of the ongoing movement.

An important aspect of the neurons recorded in area F2 is that they showed very similar properties to those previously described in area F5 (Rizzolatti and others 1988; Murata and others 1997). Therefore, it has been advanced that both areas F2 and F5 may collaborate in the control of grasping actions. In this respect, Raos and
other (2004) pose an interesting question. That is, why are 2 premotor areas involved in grasping actions? These authors (Raos and others 2004) posited that area F5 is chiefly concerned with the selection of the most appropriate type of grip. This motor representation is then supplied to area F2 whose grasping neurons keep memory of the selected motor representation as to continuously update the configuration and orientation of the hand as it approaches the object to be grasped.

The Primary Motor Cortex

The primary motor cortex (M1) and its descending projection to the spinal cord in the corticospinal tract (CST) are crucial for the normal control of hand and finger movements (Muakkassa and Strick 1979; Godschalk and others 1984; Matelli and others 1986; Dancause and others 2006). In monkeys, CST lesions produce a transient weakness, although a persistent inability to perform fine, relatively independent finger movements also occurs (Lawrence and Kuypers 1968). Similar deficits are observed temporarily during reversible inactivation of the monkey M1 hand representation (Kubota 1996; Schieber and Poliaikov 1998; Brochier and others 1999).

Interestingly, subpopulations of neurons in the M1 that project to motoneurons that innervate hand muscles are active while conducting a precision grip but not during a power grip, although their target muscles may be activated either grasp (Muir and Lemon 1983). As such, this indicates that the control of fingertip actions with a precision grip engages neural circuits that are different to those engaged during the phylogenetically older power grip (Napier 1980).

Recently much attention has been focused on the interactions between the M1 and area F5. For instance, a study aimed at understanding the unique functional contribution to grasp of M1 and PMv (area F5) recording activity of M1 and F5 neurons during the same reach-to-grasp behavior (Umiltà and others 2007). Many of these recordings were made simultaneously, using separate microdrives to record from each area. The results suggest that the populations of neurons tested play different roles at different times. F5 seems to be more involved in the premovement and early movement phases, and this activity is a strong predictor of activity later in the task. In contrast, the contribution of M1 neurons varies during different phases of the tasks. This suggests that M1 neuronal activity might be functionally quite diverse and that such different patterns of activity are required from the hand and digit muscles during grasp (Brochier and others 2004).

Human Research

Functional Neuroimaging and TMS

Functional neuroimaging and TMS studies have been conducted on humans to demonstrate the existence of and to localize cortical grasping areas similar to those described in monkeys (for review, see Castiello 2005; Culham and others 2006; Cavina-Pratesi and others 2007; Kroliczak and others 2007; Tunik and others 2007). In neuroimaging studies, participants were requested to reach toward and grasp objects of different sizes and shapes while scanned (Fig. 1C). In TMS studies, virtual lesions were elicited by applying TMS on the human anterior intraparietal sulcus (hAIP) before and after movement onset (Fig. 1D). To our knowledge, no studies have applied TMS to PMv and PMd during reach-to-grasp movements.

Posterior Parietal Cortex

A consistent result across PET and fMRI studies is the activation of a grasp-specific region within the hAIP that has been proposed as the putative homologue of the macaque area AIP (Grafton and others 1996; Faillenot and others 1997; Binkofski and others 1998; Culham and others 2003; Culham 2004; Frey and others 2005; Begliomini and others 2007b). Specifically, the focus of activation was located at the junction of the hAIP with the postcentral sulcus within the left hemisphere of subjects performing a grasping action with the right hand (Fig. 3A).

Similarly, a series of TMS studies targeting hAIP (Fig. 4A), as subjects reach-to-grasp objects, confirmed the role of hAIP in the dynamic control of grasp (Glover and others 2005; Tunik and others 2005; Rice and others 2006). For instance, Tunik and others (2005) conducted an experiment in which TMS pulses were delivered to hAIP as subjects reach-to-grasp a rectangular object (Fig. 4B). A fast motor device was used to rotate the target object, on a trial-by-trial basis, on randomly selected trials, from an initial horizontal orientation. Results indicated that TMS to the hAIP site, and not to any other cortical sites, produced a delay in the adaptive response for the perturbed (i.e., trials in which the objects were rotated) relative to the unperturbed trials. This effect was contingent on the timing of the TMS pulse being locked to the occurrence of the perturbation and was not evident when TMS was delivered at large delays after the perturbation, near the time of object contact. TMS-induced delay in adaptation was present for adapting the grasp aperture, and only the time required to actually grasp the object was affected by the TMS, not the time required to reach the target. The data from this experiment confirm the involvement of hAIP in grasping and suggest that the hAIP may perform iterative comparisons during an ongoing movement between an efference copy of the motor command and the incoming sensory information to ensure that the current grasp plan matches the current context and sensorimotor state. Therefore, hAIP is not solely a look-up table for determining grasp configurations based on perceptual features, but it has a broader role in the dynamic control of actions.

Although these findings contribute noticeably to our understanding of the neural circuit underlying grasping in humans, they leave open the question of whether hAIP has a special role in the coding of grasp type. This is because in these studies only one type of grasp was considered, namely, precision grip. One fMRI study in our laboratory considered reach-to-grasp movements...
toward objects differing in size, and subjects were not instructed on how to grasp the object (Begliomini and others 2007b). This brought to the execution of a natural precision grip movement (PG; opposition of index finger and thumb) for small objects (Fig. 5A) and a natural whole hand grasp (WHG) for large objects (Fig. 5A). Significant activity was detected within hAIP for PG but not for WHG tasks (Fig. 5B).

Although suggestive of differential activity within a key grasping area depending on the type of performed grasp, the different pattern of activation for the 2 types of grasp could have arisen from the different sizes of the stimuli and not from the diverse postures assumed by the hand. Indeed, physiological studies have reported a subset of neurons within AIP that respond to the visual presentation of 3D objects in the absence of action (Taïrta and others 1990; Sakata and Kusunoki 1992; Murata and others 2000). Therefore a second experiment was performed in which the critical manipulation was the use of the same object while instructing the subjects to use different grips (Fig. 5A; Begliomini and others 2007a). Subjects were requested to reach toward and grasp a small or a large stimulus naturally or with a constrained grasp (i.e., a PG for a large stimulus and a WHG for a small stimulus). As previously found (Begliomini and others 2007b), the hAIP was more active for PG than for WHG independently of stimulus size (Fig. 5C). Altogether these findings may indicate that a larger number of PG than WHG configurations is represented within hAIP. Therefore in humans, as in macaques, activity within this area seems to be tuned to type of grasp.

**Ventral Premotor Cortex**

Neuroimaging findings demonstrating brain activity related to the PMv during a reach-to-grasp movement have so far been lacking. These essentially null findings, which contrast with the strong involvement of PMv for grasping movements in macaques (e.g., Rizzolatti and...
Fig. 4. Examples of transcranial magnetic stimulation (TMS) reach-to-grasp experiments and stimulated regions. 

A, Location of stimulation to human anterior intraparietal sulcus (hAIP). 

B, Effect of TMS on online control of grasp as a function of aperture size. Reach-to-grasp adjustments required in the experiment by Tunik and others (2005) in which the TMS pulse was delivered to the hAIP. In most trials, the object rotated 180 degrees (unperturbed), leaving the grasp aperture unperturbed. In a minority of trials, the object rotated 90 degrees (perturbed) necessitating an increase in grasp aperture. Aperture profiles in the unperturbed and perturbed conditions are plotted as hatched and solid lines, respectively. Trials in which TMS is delivered early and late are plotted in blue and red, respectively. Vertical lines indicate, respectively, T1: onset of early TMS pulse; T2: onset of late TMS pulse; M: time of motor rotation. Note that the aperture profiles of the early- and late-TMS conditions diverged from each other in the size-perturbed condition. Stimulation of hAIP caused variations in grip scaling in response to the object size perturbation. 

C, Location of stimulation to the primary motor cortex (M1). 

D, TMS experiment by Lemon and others (1995) and the behavioral performance showed by participants included in the study. 

D1, Position of the markers for kinematic registration: top of test object; nail of index finger; nail of thumb; wrist. The TMS pulse was delivered during mid-reach, late-reach, or pre-touch phases, and it was triggered online from spatial coordinates of the index finger marker. 

D2, Curves indicate marker trajectories superimposed from consecutive trials carried out by a single subject. Modified and reprinted from Tunik and others (2007); Lemon and others (1995) with the permission of Elsevier and the Society for Neurosciences, respectively.
could be due to several possibilities. For one, there may be interspecies differences in the organization of the PMv. The development of a motor speech area in humans may have changed the location of the human functional homologue of monkey area F5 (Amunts and Zilles 2001). For another, it is customary to isolate grasping-related activations by subtracting activations obtained during the reaching-only tasks from the reach-to-grasp tasks. As such, both the reaching and the grasping tasks require specific motor goals, which usually trigger premotor activations. Consequently, activations within the PMv may have canceled one another when compared (Grafton and others 1996; Culham and others 2003; Frey and others 2005; Begliomini and others 2007b; Begliomini and others 2007a).

**Dorsal Premotor Cortex**

In humans, the contribution of the PMd to hand movements, the time course of its involvement, and its hemispheric dominance is essentially unknown. One study from our laboratory (Begliomini and others 2007a), however, found some evidence of bilateral PMd activity presiding the control of visually guided hand-grasping actions. Specifically, the bilateral PMd activation was evident when subjects performed constrained grasps (Fig. 5D). The increase of activity within the PMd for specific grasp types

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**Fig. 5.** Brain regions when right-handed participants perform natural or constrained visually guided grasping movements. A, Photographs representing the types of grasp adopted by Begliomini and others (2007a). B, Significant changes of brain activity observed within the left pre- and post-central gyri for both precision grip small stimulus (PGS) and whole hand grasp large stimulus (WHGL). Activations in human anterior intraparietal sulcus (hAIP) appear to be selective for PGS (areas colored in purple indicate the overlap between the 2 activation maps). C, For constrained grasping movements (precision grip large stimulus [PGL], whole hand grasp small stimulus [WHGS]), activations are detected in both pre- and post-central gyri. hAIP activations are confined to PGL (bluish areas indicate overlap between the 2 areas). D, Depicts brain activations obtained for natural (green color) and constrained (red color) conditions (see A). The execution of constrained movements leads to bilateral activity involving also the dorsal premotor cortex. Conventions as in Figure 3.
seems to provide the evidence that, in humans as in monkeys (Raos and others 2004), this area is involved in the control of grasping movements. In particular, PMd activity seems to play a crucial role in monitoring the configuration of fingers during planning and execution of grasping actions.

**Primary Motor Cortex**

Obviously activity in M1 has consistently been found during reach-to-grasp tasks (e.g., Grafton and others 1996; Faillenot and others 1997; Culham and others 2003; Begliomini and others 2007b). However, a systematic documentation of neuronal activity in the M1 when subjects reach toward and grasp real objects using different grip configurations has yet to be provided. Recent fMRI findings, however, seem to suggest that activity in the M1 is modulated by the level of congruence between type of grasp and stimulus size (Begliomini and others 2007a; Begliomini and others 2007b). Of interest is that a similar pattern of activity was found for the PMd. This result seems to confirm previous neurophysiological evidence suggesting that the PMd may control the execution of grasping actions through their direct connections with the M1 (Raos and others 2004). In keeping with these lines of evidence, it might well be that the PMd representation of stimulus size-specific grasp is transformed within the M1 to recruit motor outputs to the hand that can modify hand shape appropriately for successful grasp and manipulation of the object (Umlità and others 2007).

A study used TMS directed toward the hand area of the M1 (Fig. 4C-D) to assess the influence of the corticospinal system on the motor output during the various phases of a task requiring the human subject to reach for an object and grasp and lift it (Lemon and others 1995). The results show that the cortical representations of extrinsic hand muscles, which act to orientate the hand and finger tips, were subjected to a strong excitatory drive throughout the reach. The intrinsic hand muscles appeared to receive their strongest cortical input as the digits closed around the object, and just after the subject touched the object at the onset of manipulation. Thus, these findings show a significant and heterogeneous variation in M1 cortical activity during the evolution of a reach-to-grasp movement.

**Lesion Studies**

The evidence for specialized circuits for grasping in the human brain comes mainly from the neuropsychological literature. To facilitate comparison across humans and monkeys, we will discuss brain areas in the sequence used above: posterior parietal cortex (PPC) and M1. To our knowledge, no reach-to-grasp studies have been conducted on patients with lesions of either the PMv and/or PMd.

**Posterior Parietal Cortex**

There is some evidence that the posterior parietal cortex has a specific role in human grasping. In line with the results obtained from monkeys in which AIP has been inactivated, Binkofski and others (1998) found that human patients with lesions in hAIP showed deficits in grasping, whereas reaching remained relatively intact. Striking evidence for a deficit in visually guided grasping has come from patients with optic ataxia (Glover 2003; Rossetti and others 2003). Optic ataxia is classically considered to be a specific disorder of the visuomotor transformation caused by posterior parietal lesions, in particular, lesions of the superior parietal lobe (SPL). Jeannerod (1986) found that in reaching to grasp an object, the finger grip aperture of patients with optic ataxia was abnormally large, and the usual correlation between maximum grip aperture and object size was missing (Fig. 6A-B). Subsequently, various patients have been described that show specific deficits in the control of grasping after damage to the SPL. Patient V.K. (Jakobson and others 1991), for example, showed an apparently normal early phase of hand opening during attempts to grasp an object, but her online control of grip aperture quickly degenerated, resulting in numerous secondary peaks in the grip aperture profile (Fig. 6C), rather than the single peak typical of a healthy subject. Patient I.G. (Milner and others 2001; Milner and others 2003) also showed considerable deficits in the scaling of her maximum grip aperture to the size of an object. Another patient, A.T. (Jeannerod and others 1994), with extensive damage to the SPL and secondary visual areas, and some damage to the inferior parietal lobule (IPL), showed exaggerated anticipatory opening of the fingers with poor correlation with object size, resulting in awkward grasps. However, this deficit was much less marked if neutral “laboratory” objects such as wooden blocks were replaced with familiar objects, such as a lipstick.

**Primary Motor Cortex**

As in the monkey, lesions of the human primary motor cortex or corticospinal fibers profoundly disrupt grasping (Denny-Brown 1950; Lassek 1954; Lang and Schieber 2004). Such lesions typically lead to grasping movements that are initially characterized by the loss of independent finger movement, although synergistic movements of all fingers (e.g., a power grip) remain intact. Independent finger movements sometimes recover later. Furthermore, lesions of these neural structures result in the syndrome of hemiparesis, in which voluntary effort produces sluggish, weakened movements. In addition, hemiparetic movements are less individuated. Attempts to move or exert force with a single finger result in simultaneous action of all the fingers, and attempts to grasp an object with the hand may result in simultaneous motion at the elbow and shoulder (Twitchell 1951; Brunstrom 1970; Lang and Schieber 2003; Latash and others 2003).

An important aspect of M1 in terms of a homology between the lesion studies in humans and the neurophysiological work described above is a somewhat greater somatotopic gradient of digit representation in the human M1 than in the macaque M1. In the macaque M1, partial inactivation of hand representation impaired some finger movements and not others, but adjacent fingers were not...
affected more readily than nonadjacent fingers, and the finger movements that were affected were not systematically related to the mediolateral location of the inactivation (Schieber and Poliakov 1998). In humans, however, small strokes can impair the thumb and index finger more than the little and ring fingers or vice versa (Schieber 1999). Moreover, the thumb and index finger are impaired more severely by more lateral lesions, and the little and ring fingers are more impaired by more medial lesions (Kim 2001). Therefore, these lesion studies, as well as the studies of neural activity described above, suggest that a somatotopic gradient of digit representation, with the thumb represented more heavily laterally and the little finger represented more heavily medially, is present in the human M1 but is not so evident in the macaque M1 hand representation. The implications for such species difference in the M1 have been reviewed elsewhere (Schieber and Santello 2004).

Conclusions and Future Directions

Some progress has been made in characterizing the kinematics of grasping and the neural substrates that underlie it. Nonetheless, much remains unknown and many important issues have yet to be addressed.

First, a complete understanding of the neural circuit underlying grasping requires information from circuits that code object meaning (inferotemporal lobe) and circuits where decisions on what to do are taken (prefrontal lobe, cingulate areas). As pointed out by Rizzolatti and Luppino (2001; see also Fagg and Arbib 1998), a fundamental issue that any model of grasping has to address is the fact that objects may be grasped in several ways. The chosen grip depends on object visual properties, but also on object meaning and on what the agent of the action wants to do with the object. Therefore, the selection of one of the possible ways of grasping does not depend exclusively on the visual intrinsic properties of the object. To this end, Fagg and Arbib (1998) proposed a revised version of the classic visuomotor circuit underlying grasping that also considers areas that are relevant for intention and decision (please refer to the red panels in Fig. 2B). This model provides physiologically testable predictions that should be taken into account in future neurophysiological and neuroimaging work. Work in humans has shown that choosing a grip does not depend exclusively on the visual properties of the object but also on the meaning attached to the object and what an individual intends to do with it (e.g., Cohen and Rosenbaum 2004; Ansuini and others 2006; Armbrüster and Spijkers 2006; Ansuini and others 2007). What is necessary is neurophysiological and functional imaging work to discover whether and to what extent such variables influence the activity of key grasping areas and the intention/decision areas hypothesized by Fagg and Arbib (1998) in both humans and monkeys.

Second, a problem for neuroscience to solve is how perceptual inputs are able to guide actions. In all reach-to-grasp studies reported here, the experimental environment contains only one object for action, whereas the environments within which we normally act contain many objects toward which action could be directed. Therefore, to exercise free choice and control, it is essential that the system have the capacity to link action selectively with particular objects. In this respect, a number of behavioral experiments have been designed to look at changes in reach-to-grasp movement kinematics when multiple objects within the workspace were introduced (for a review, see Tipper.
and others 1998; Castiello and others 1999). In these circumstances, actions appear to be prepared for all potential target objects with the result that grasp kinematics were affected by the presence of the nontarget objects. Thus, it is reasonable to assume that the neural network underlying reach-to-grasp actions is likely to represent more than just the target object for action. To date, only one fMRI study investigated whether there is a different level of activation for key grasping areas when action may be prepared to all candidate target objects (Chapman and others 2007). Specifically, parallel processing of stimuli for action determined an increase of activity within the M1 and the pre-cuneus (PCu). Of interest is that the PCu has been suggested as a putative homologue of the monkey parietal reach reaching area (PRR), which includes macaque area V6A, which has been proposed to be involved not only in reaching but also in grasping movements (Gallelli and others 2003). Further neurophysiological and functional imaging studies are needed to investigate the process of perceptual selection for the control of hand actions in both monkeys and humans.

Third, whereas the neural circuit concerning the visuomotor transformations underlying grasping has been given great attention (Jeannerod and others 1995; Rizzolatti and Luppino 2001), much less attention has been paid to the contribution to grasping of subcortical structures such as the basal ganglia and the cerebellum. Lesion, imaging, and electrophysiological evidence shows that the cerebellum and the basal ganglia are involved in the signaling of hand kinematics during prehension. Cerebellar patients (e.g., Haggard and others 1994; Lang and Bastian 1999; Rand and others 2000; Timmann and others 1999, 2001; Zackowski and others 2002) and patients with basal ganglia disorders such as Parkinson’s and Huntington’s disease (e.g., Castiello and others 1993; Bennett and others 1995; Weiss and others 1997; Bonfiglioli and others 1998; Schettino and others 2006) exhibit a spectrum of kinematic impairments in the learning, planning, and execution of prehensile movements, which are consistent with the proposal that the cerebellum and the basal ganglia play a major role in the control and coordination of reach-to-grasp movements. Furthermore, neurophysiological work has identified various cerebellar (Smith and others 1993; Gibson and others 1994; van Kan and others 1994; Mason and others 1998; Mason and other 2006) and basal ganglia (Wenger and others 1994; Wannier and others 2001) structures implicated in the kinematics of reach-to-grasp movements. Although functional imaging reach-to-grasp studies reported cerebellar activations (Grafton and others 1996; Rizzolatti and others 1996; Chapman and others 2002; Beglomini and others 2007b), they are poorly discussed. Therefore, what would be needed is a thorough investigation of cerebellar and basal ganglia activation in humans and their implications for the planning and execution of reach-to-grasp movements. This would add an additional layer of complexity to the process involved in the transformation of the visual properties of a 3D object into the appropriate hand movement to manipulate that object as outlined below. Indeed, recent developments in the investigation of the anatomical connections between key grasping areas of the visuomotor circuit and subcortical structures make this a timely and tractable issue. A series of studies using retrograde transneuronal transport of viruses has revealed basal ganglia and cerebellum inputs to AIP and PMv (Hoover and Strick 1993; Clower and others 2001; Dum and Strick 2002; Clower and others 2005). For instance, Clower and others (2001) revealed that the AIP, PMv, and M1 are the targets of inputs coming from both the basal ganglia and cerebellum, in particular, from the substantia nigra (caudal part) and the internal segment of the globus pallidus for the basal ganglia (Hoover and Strick 1993, 1999) and for the dentate nucleus (medial-caudal part) of the cerebellum (Clower and others 2001; Dum and Strick 2002, 2003). In this respect, the fast development of neuroimaging techniques might allow researchers to determine how the various grasping-related areas in the human brain are connected. Specific imaging techniques (such as diffusion tensor imaging, DTI; Basser and Pajevic 2000; Ramnani and others 2004) allow us to illuminate the connections between different points of the magnetic resonance image. DTI could be used for in vivo anatomical mapping of the axonal connections between areas that are involved in grasping.

Fourth, the idea of combining different techniques might be the best way forward when it comes to comparing grasping in humans and nonhuman primates. Ideally, a coordinated series of neuroimaging experiments should be implemented in humans and monkeys. Being able to put both species in the same position would minimize postural and morphological differences. In addition, MRI-compatible systems now make possible electrophysiological and possibly kinematic recording in both species during scanning (Logothetis and others 1999; Nelissen and others 2005).

Finally, the issue of lateralization concerning reach-to-grasp-related activation needs further development. Although behavioral evidence (Grosskopf and Kuhtz-Buschbeck 2006; Gonzalez and others 2007) is starting to reveal functional hemispheric asymmetries for the control of reach-to-grasp movements, very little work has been done in terms of neural correlates. To our knowledge, only one fMRI experiment with reaching and grasping using the left and right hands has been conducted (Culham and others 2001). Grasping with either hand led to bilateral hAIP activation; however, both the extent and the magnitude of activation were much larger in the hemisphere contralateral to the hand used. In addition to hAIP, the supplementary motor area in the medial frontal cortex was activated bilaterally and the PCu was significantly activated only by right-handed grasping. Further functional imaging work is necessary to uncover the neural control of each hand for reach-to-grasp tasks. The main questions to be addressed should concern the relationship between the use of dominant and nondominant hand with respect to the position in which the to-be-picked-up objects are located and whether there is a hemispheric specialization with respect to the type of adopted grasp (Gonzalez and others 2007).
In conclusion, although much is now known about the neural substrates of grasping, much remains to be discovered. Recent methodological advances should allow more direct examination of the possible human homologues of grasping areas identified in monkeys, as well as the identification and parcellation of areas that might be uniquely human. It will only be through careful and thoughtful experimentation, using converging techniques, that we might completely understand the grasping function of the human hand.

Further research will be needed to better understand the central neural systems that control the hand. Understanding control of the hand may find application in various domains. For instance, the design and implementation of neural prostheses (Donoghue 2002; Taylor and others 2002) that might drive functional electrical stimulation to restore hand function after spinal cord injury would be greatly facilitated by a more detailed knowledge of the hand’s normal biological control. The advantages provided by the biological system may also provide insights for engineering more dexterous robotic hands. Finally, hand surgery (Valero-Cuevas and Hentz 2002), rehabilitation for functional recovery after hand reattachment or transplantation surgery (Giroux and others 2001; Jones 2002; Dubernard and others 2003), as well as after stroke or other central lesions (Lang and Schieber 2003; Li and others 2003) would also benefit from this research.

References


