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# 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

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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.

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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; Fagg and Arbib 1998). Then the representation of 3D object features influences both the dorsal and ventral premotor areas of the frontal lobe (PMd and PMv, respectively), which are known to be important for visual guidance of the hand (Moll and Kuypers 1977; Godschalk and others 1981; Weinrich and Wise 1982; Passingham 1987; Rizzolatti and others 1988; Raos and others 2004). The PMv plays a primary role in selecting the most appropriate type of grip on the basis of the object affordances provided by AIP to which it is reciprocally connected, thus activating a motor representation of the object. This motor representation is then supplied to the PMd, which keeps memory of it and combines it with visual information provided by cortical areas of the superior parietal lobe to continuously update the configuration and orientation of the hand as it approaches the to-be-grasped object. The final output for action execution most likely involves both PMv and PMd. The represented action is initially coded globally.

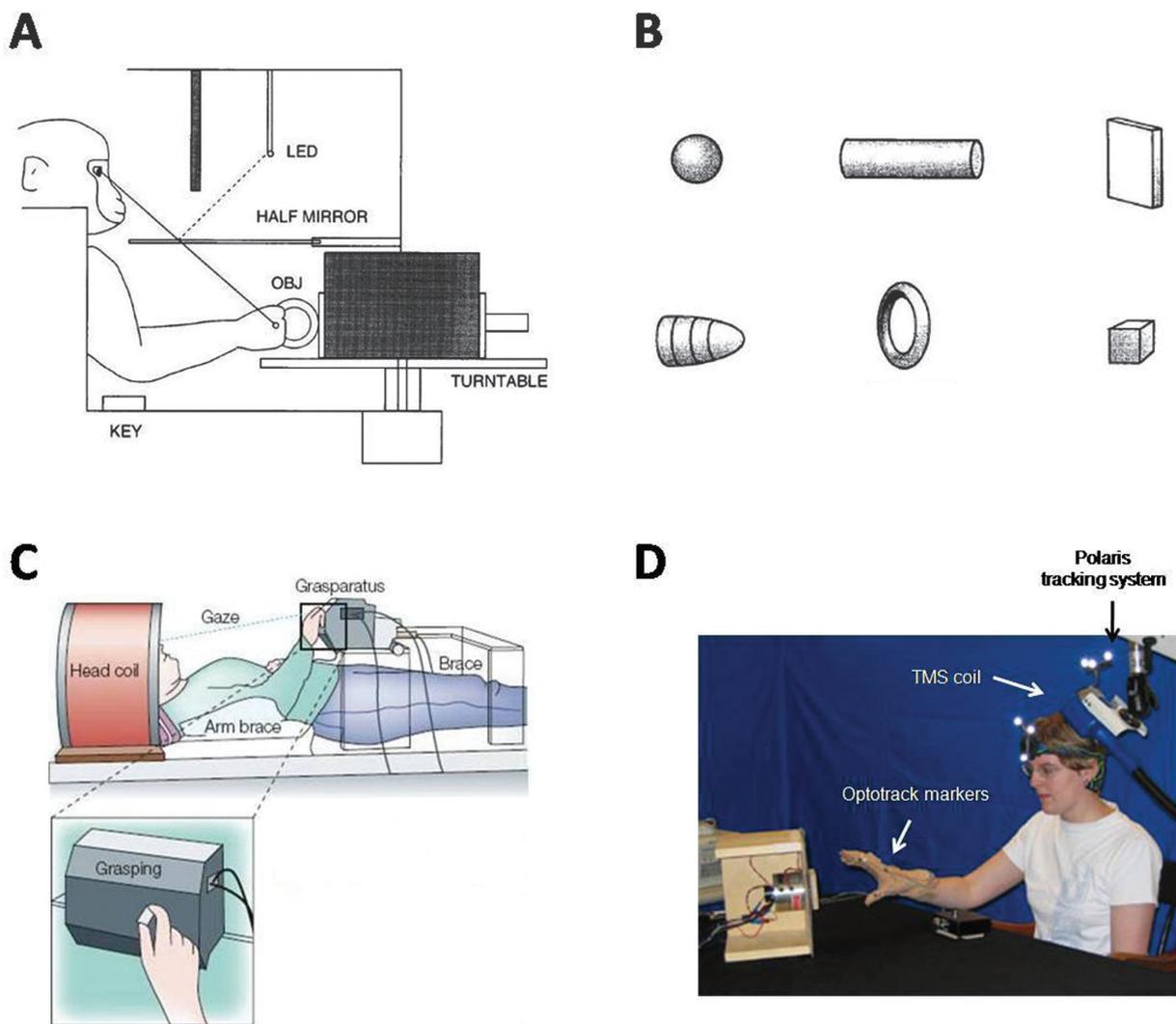
Then, it is temporally segmented and sent to the hand primary motor cortex (M1) for motor execution. This system is depicted in Figure 2A and 2B (blue panels), and the specific properties of the neurons within each of the areas composing this system are described within the following sections.

### *Posterior Parietal Cortex*

The first insight into neural substrates for the visual control of hand movements came from electrophysiological studies in macaque monkeys, showing “hand-manipulation” neurons in area 7 of the inferior parietal lobule (IPL; Hyvarinen and Poranen 1974; Mountcastle and others 1975). For example, Mountcastle and others (1975) observed parietal neurons that were active when the monkey actively manipulated an object, but not during passive stimulation of the arms or hand.

Subsequent electrophysiological research revealed that neurons involved in hand movements were found to be concentrated in a small zone within the rostral part of the posterior bank of the intraparietal sulcus, corresponding to the AIP. Neurons from this area were recorded in monkeys trained to grasp various types of objects (Fig. 1B) that elicited different motor configurations. The activity of these neurons was not influenced by changing the position of the object in space, showing that the activity was related to distal hand and finger movements rather than to proximal movements of the arm. According to Sakata and colleagues (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) (Gallese 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



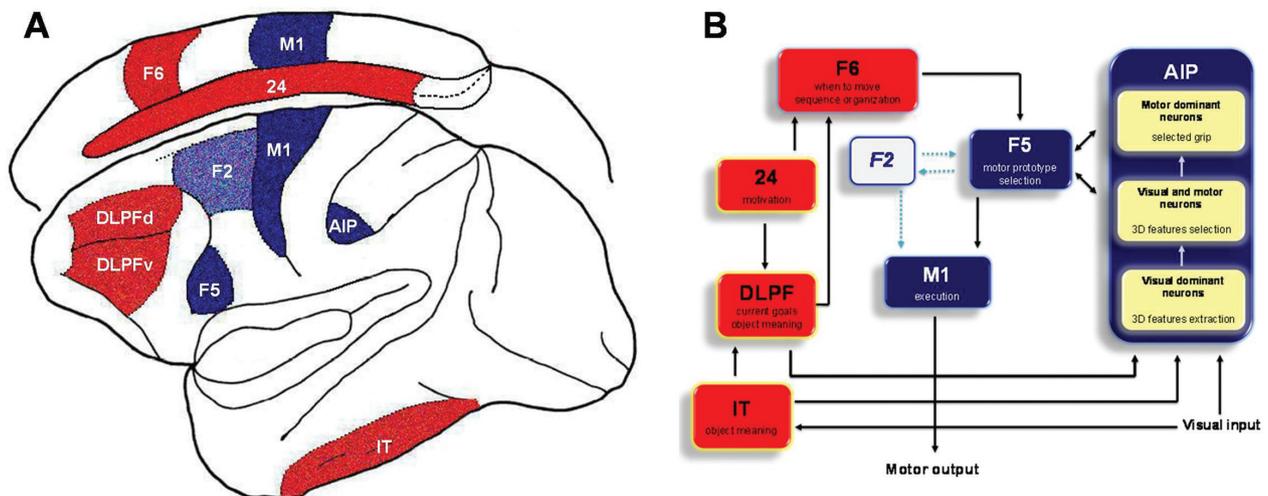
**Fig. 1.** Example of methods used to investigate grasping movements in humans and monkeys. *A*, Experimental setup adopted by neurophysiologists to investigate neural activity related to visually guided reach-to-grasp movements in monkeys. The monkey is seated in front of a box, which houses 6 different objects (*B*). Objects are presented one at a time in a central position in random order by a turntable. A red spot of light from a red/green light-emitting diode (LED) is projected onto the object, and the monkey is required to fixate it and press a key. Key pressing turns on the light inside the box and makes the object visible. After the monkey presses the key for 1.0 to 1.2 s, the LED changes color (green, go signal) and the monkey is allowed to release the lever and grasp the object. *C*, The “grasparatus” used for functional MRI studies by Culham and others (2003). A metal-free device that allows a computerized presentation of a wide range of real 3D stimuli. The grasparatus consists of an octagonal rotating drum with 4 translucent rectangular 3D shapes on each of 8 faces. The grasparatus could be rotated to each of the 8 faces between trials using a computer-controlled pneumatic system. *D*, Setup for transcranial magnetic stimulation (TMS) reach-to-grasp studies. A polaris tracking system allows for alignment between the TMS coil on the head and the high-resolution anatomical scan of the participant’s brain. Optotrak markers are used to record hand movements. Modified and reprinted from Castiello (2005), Murata and others (2000) with permission from the Nature Publishing Group and the American Physiological Society. We thank Dr. Hamilton for allowing us to publish the modified photograph represented in panel *D*.

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,



**Fig. 2.** The visuomotor grasping circuit. *A*, Lateral view of the monkey cerebral cortex. Areas highlighted in blue represent those areas composing the “classic” visuomotor grasping circuit. Area F2 is highlighted in light blue given that its specific contribution in visually guided grasping and its connections to other brain areas of the visuomotor grasping circuit is still under debate. Areas highlighted in red represent those areas that may be involved in intentional and decisional aspects underlying the planning and execution of grasping. *B*, Schematic model of visuomotor transformation for grasping. Conventions as for panel A. M1 = primary motor cortex; AIP = anterior intraparietal sulcus; DLPF = dorsolateral prefrontal; IT = inferotemporal. Modified and reprinted from Rizzolatti and Luppino (2001) and Fagg and Arbib (1998) with permission from Elsevier.

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 2001) 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

others (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 Poliakov 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 in 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*

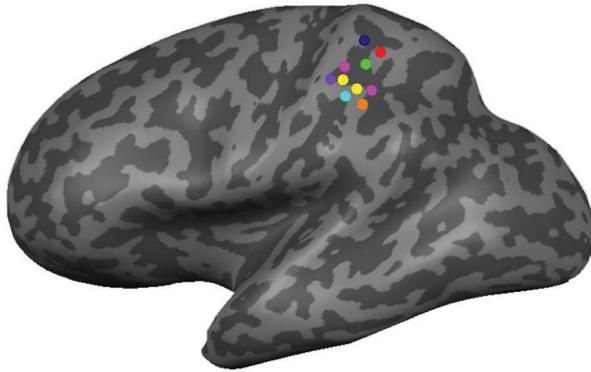
A consistent result across PET and fMRI studies is the activation of a grasp-specific region within the hAIP that has been proposed as the putative homologue of the macaque area AIP (Grafton and others 1996; Faillenot and others 1997; Binkofski and others 1998; Culham and others 2003; Culham 2004; Frey 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.

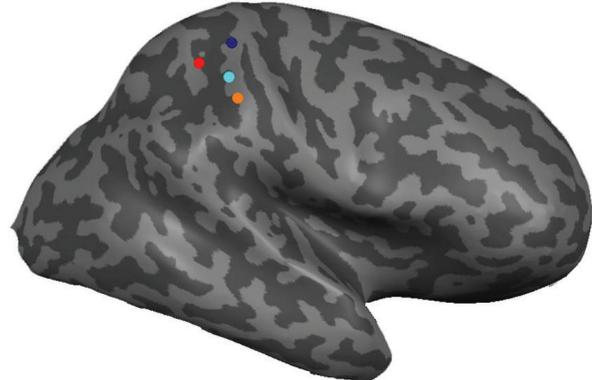
Although these findings contribute noticeably to our understanding of the neural circuit underlying grasping in humans, they leave open the question of whether hAIP has a special role in the coding of grasp type. This is because in these studies only one type of grasp was considered, namely, precision grip. One fMRI study in our laboratory considered reach-to-grasp movements



### A Left hemisphere



### B Right hemisphere



### C

Studies	Left hemisphere	Right hemisphere
Grafton and others, 1996	-33 -41 55	33 -43 60
Binkofski and others, 1998	-40 -40 40; -45 -35 43	
Culham and others, 2003	-38 -48 52	40 -50 50
Frey and others, 2005	-40 -33 43	
Begliomini and others, 2007b	-36 -45 38; -33 -36 48	
Cavina-Pratesi and others, 2007	-37 -42 36	39 -39 38
Kroliczak and others, 2007	-47 -34 37	43 -37 42
Begliomini and others, 2007a	-33 -42 49	

**Fig. 3.** Meta-analysis of hAIP activations. *A*, Human anterior intraparietal sulcus (hAIP) activations reported from imaging studies (fMRI and PET) for the left hemisphere. *B*, hAIP activations reported from imaging studies for the right hemisphere. These activations were detected during visually guided reach-to-grasp movements performed with the right hand. Colored dots indicate activation peaks according to the coordinates reported in various studies. Activations are superimposed on a normalized single-subject high-resolution anatomical scan. Images are displayed in neurological convention. *C*, List of studies reporting hAIP activations together with the locations expressed in Talairach coordinates.

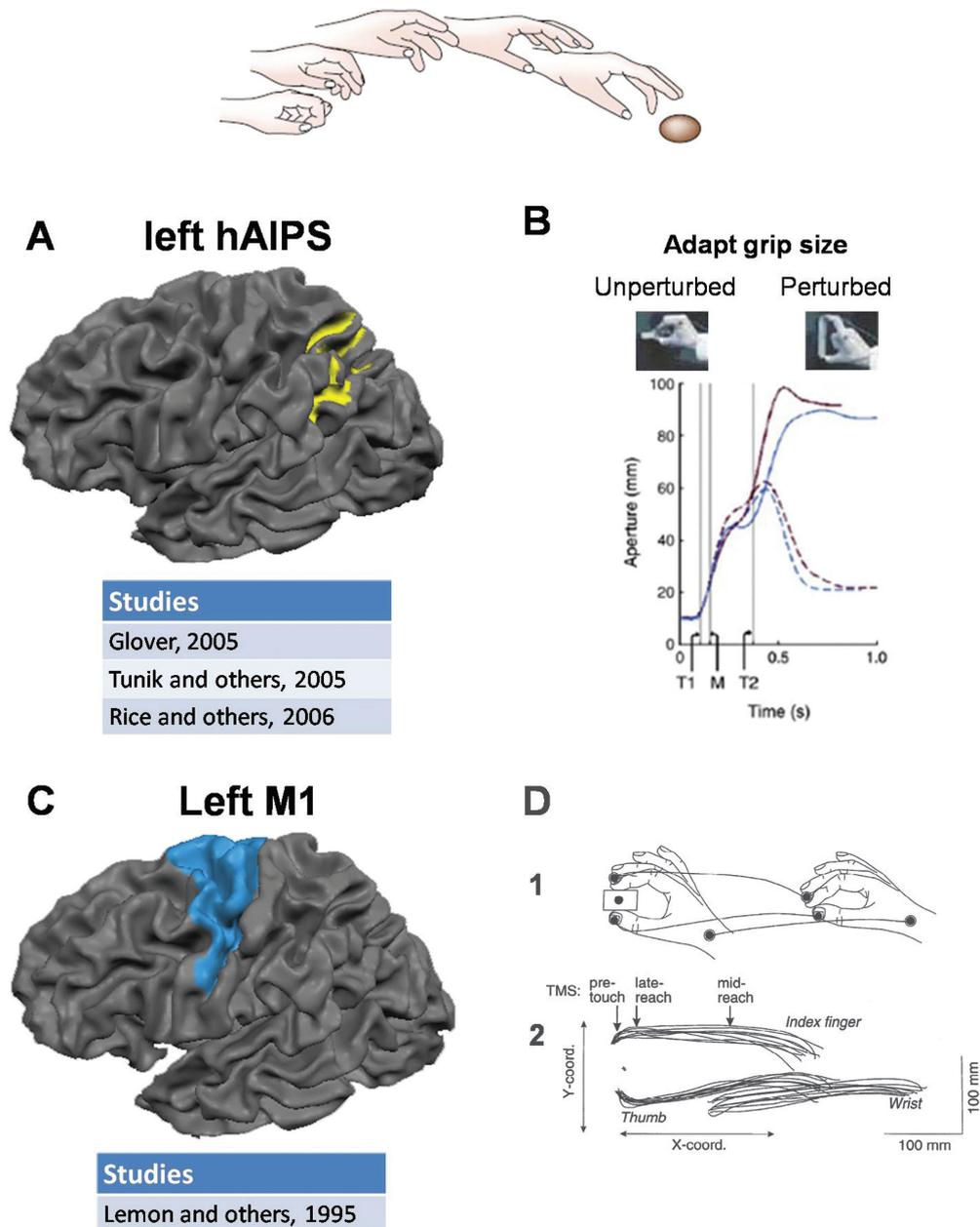
toward objects differing in size, and subjects were not instructed on how to grasp the object (Begliomini and others 2007b). This brought to the execution of a natural precision grip movement (PG; opposition of index finger and thumb) for small objects (Fig. 5A) and a natural whole hand grasp (WHG) for 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 (Taira 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

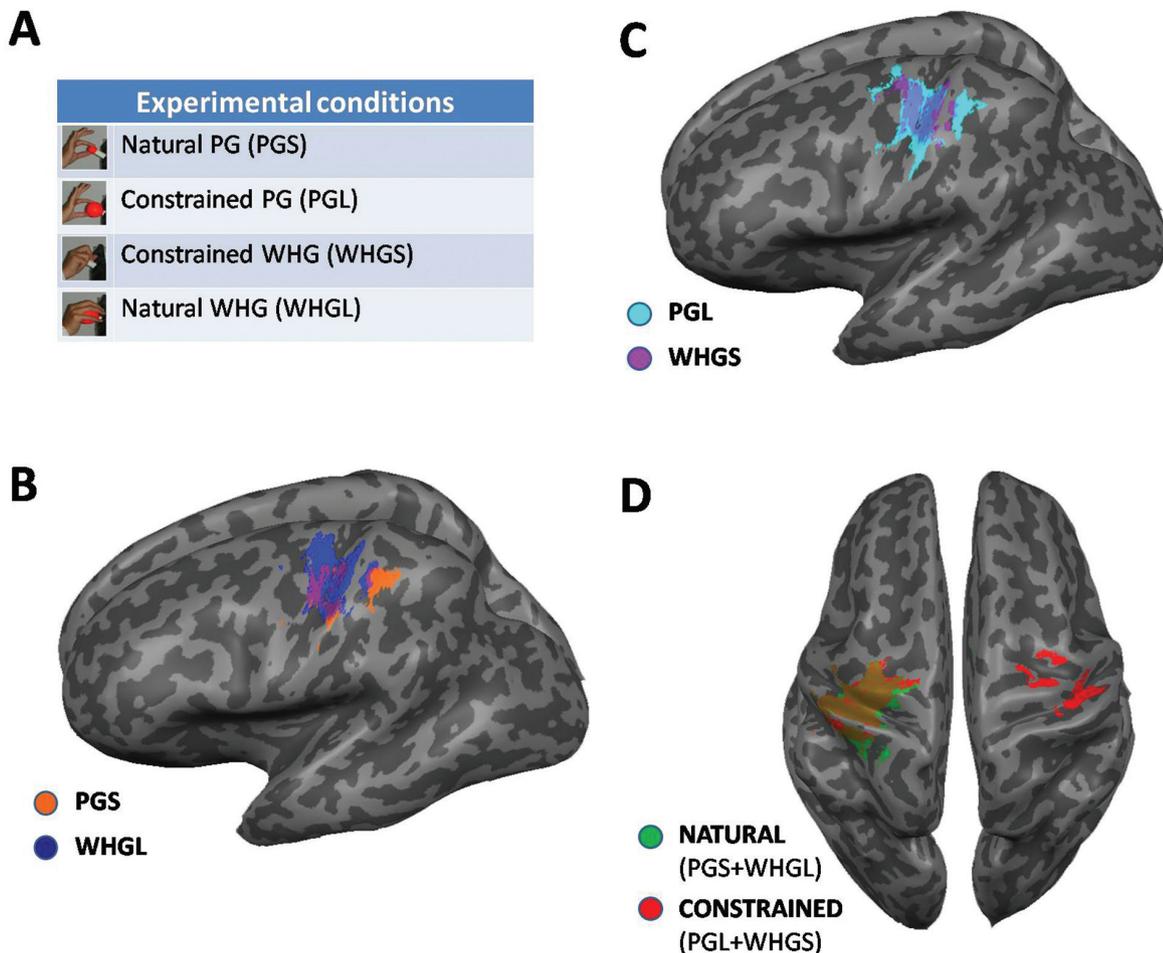
object while instructing the subjects to use different grips (Fig. 5A; Begliomini and others 2007a). Subjects were requested to reach toward and grasp a small or a large stimulus naturally or with a constrained grasp (i.e., a PG for a large stimulus and a WHG for a small stimulus). As previously found (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.



**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.

others 1988), 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. 5*D*). The increase of activity within the PMd for specific grasp types

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 (Umiltà 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

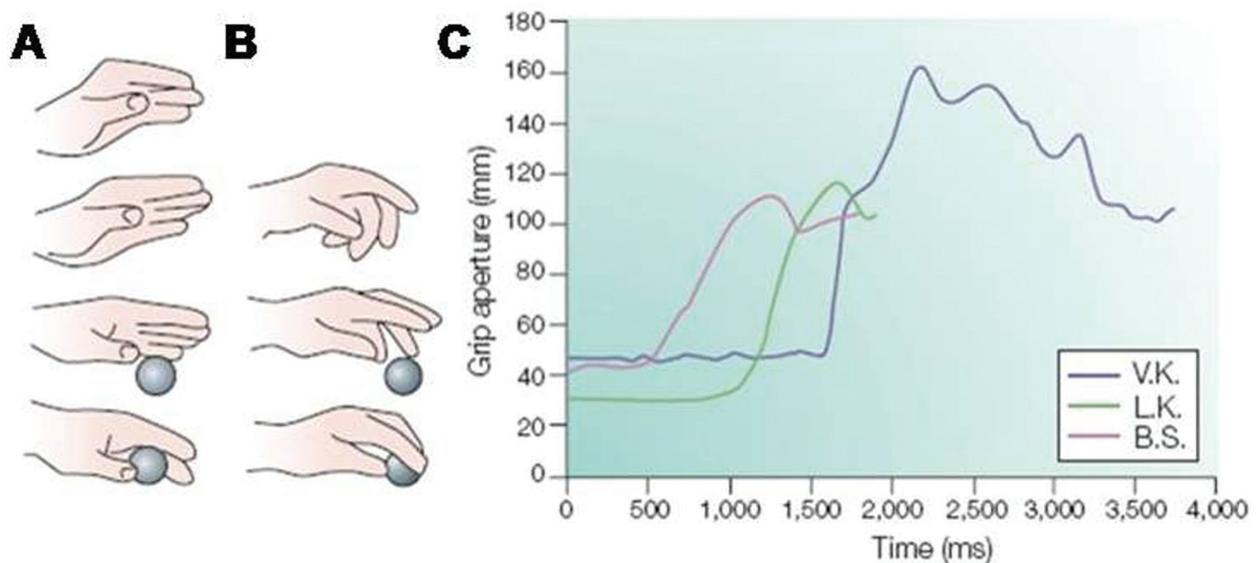
results obtained from monkeys in which AIP has been inactivated, Binkofski and others (1998) found that human patients with lesions in hAIP showed deficits in grasping, whereas reaching remained relatively intact.

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; Brunnstrom 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



**Fig. 6.** Grip aperture profiles of patients with brain damage. Comparison of the pattern of finger grip in a patient with optic ataxia during reaching with the affected hand (A) and the normal hand (B). C, Comparison of the abnormal pattern of finger grip in a patient (V.K.) with the pattern of finger grip of 2 neurologically healthy participants (L.K. and B.S.). Modified and reprinted from Castiello (2005), with the permission of Nature Publishing Group.

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 (Galletti 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 1999; 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; Begliomini 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* (medio-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 Kutz-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 parcelation 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 (Giraux 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

- Amunts K, Zilles K. 2001. Advances in cytoarchitectonic mapping of the human cerebral cortex. *Neuroimaging Clin North Am* 11:151–69.
- Ansuini C, Giosa L, Turella L, Altoè G, Castiello C. 2007. An object for an action, the same object for other actions: effects on hand shaping. *Exp Brain Res*. [Epub ahead of print]
- Ansuini C, Santello M, Massaccesi S, Castiello U. 2006. Effects of end-goal on hand shaping. *J Neurophysiol* 95:2456–65.
- Armbrüster C, Spijkers W. 2006. Movement planning in prehension: do intended actions influence the initial reach and grasp movement? *Motor Control* 10:311–29.
- Bandettini PA, Jesmanowicz A, Wong EC, Hyde JS. 1993. Processing strategies for time-course data sets in functional MRI of the human brain. *Magn Reson Med* 30:161–73.
- Basser PJ, Pajevic S. 2000. Statistical artifacts in diffusion tensor MRI (DT-MRI) caused by background noise. *Magn Reson Med* 44:41–50.
- Begliomini C, Caria A, Grodd W, Castiello U. 2007a. Comparing natural and constrained movements: new insights into the visuomotor control of grasping. *PLoS ONE*. 2:e1108.
- Begliomini C, Wall MB, Smith AT, Castiello U. 2007b. Differential cortical activity for precision and whole-hand visually guided grasping in humans. *Eur J Neurosci* 25:1245–52.
- Bennett KM, Marchetti M, Iovine R, Castiello U. 1995. The drinking action of Parkinson's disease subjects. *Brain* 118:959–70.
- Binkofski F, Dohle C, Posse S, Stephan KM, Hefter H, Seitz RJ, and others. 1998. Human anterior intraparietal area subserves prehension: a combined lesion and functional MRI activation study. *Neurology* 50:1253–9.
- Bonfiglioli C, De Berti G, Nichelli P, Nicoletti R, Castiello U. 1998. Kinematic analysis of the reach to grasp movement in Parkinson's and Huntington's disease subjects. *Neuropsychologia* 36:1203–8.
- Brochier T, Boudreau MJ, Pare M, Smith AM. 1999. The effects of muscimol inactivation of small regions of motor and somatosensory cortex on independent finger movements and force control in the precision grip. *Exp Brain Res* 128:31–40.
- Brochier T, Spinks RL, Umilta MA, Lemon RN. 2004. Patterns of muscle activity underlying object-specific grasp by the macaque monkey. *J Neurophysiol* 92:1770–82.
- Brunnstrom S. 1970. *Movement therapy in hemiplegia: a neurophysiological approach*. New York: Medical Department, Harper & Row.
- Caminiti R, Johnson PB, Galli C, Ferraina S, Burnod Y. 1991. Making arm movements within different parts of space: the premotor and motor cortical representation of a coordinate system for reaching to visual targets. *J Neurosci* 11:1182–97.
- Castiello U. 2005. The neuroscience of grasping. *Nat Rev Neurosci* 6:726–36.
- Castiello U, Bennett K, Bonfiglioli C, Lim S, Peppard RF. 1999. The reach-to-grasp movement in Parkinson's disease: response to a simultaneous perturbation of object position and object size. *Exp Brain Res* 125:453–62.
- Castiello U, Bennett KM, Adler CH, Stelmach GE. 1993. Perturbation of the grasp component of a prehension movement in a subject with hemiparkinson's disease. *Neuropsychologia* 31:717–23.
- Cavina-Pratesi C, Goodale MA, Culham JC. 2007. fMRI reveals a dissociation between grasping and perceiving the size of real 3D objects. *PLoS ONE* 2:e424.
- Chapman H, Gavrilesu M, Wang H, Kean M, Egan G, Castiello U. 2002. Posterior parietal cortex control of reach-to-grasp movements in humans. *Eur J Neurosci* 15:2037–42.
- Chapman H, Pierno AC, Cunnington R, Gavrilesu M, Egan G, Castiello U. 2007. The neural basis of selection-for-action. *Neurosci Lett* 417:171–5.
- Clower DM, Dum RP, Strick PL. 2005. Basal ganglia and cerebellar inputs to 'AIP'. *Cereb Cortex* 15:913–20.
- Clower DM, West RA, Lynch JC, Strick PL. 2001. The inferior parietal lobule is the target of output from the superior colliculus, hippocampus, and cerebellum. *J Neurosci* 21:6283–91.
- Cohen RG, Rosenbaum DA. 2004. Where grasps are made reveals how grasps are planned: generation and recall of motor plans. *Exp Brain Res* 157:486–95.
- Culham J. 2004. Human brain imaging reveals a parietal area specialized for grasping. In: Duncan J, Kanwisher N, editors. *Attention and performance: functional neuroimaging of visual cognition*. Oxford (UK): Oxford University Press. p 417–38.
- Culham JC, Cavina-Pratesi C, Singhal A. 2006. The role of parietal cortex in visuomotor control: what have we learned from neuroimaging? *Neuropsychologia* 44:2668–84.
- Culham JC, Danckert SL, DeSouza JF, Gati JS, Menon RS, Goodale MA. 2003. Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Exp Brain Res* 153:180–9.
- Culham JC, Woodward SL, Milner AD, Gati JS, Menon RS, Goodale MA. 2001. Laterality of fMRI activation in AIP during grasping and imagined grasping of visual targets. Paper presented at the Society for Neuroscience, San Diego, CA.
- Dancause N, Barbay S, Frost SB, Plautz EJ, Popescu M, Dixon PM, and others. 2006. Topographically divergent and convergent connectivity between premotor and primary motor cortex. *Cereb Cortex* 16:1057–68.
- Denny-Brown D. 1950. Disintegration of motor function resulting from cerebral lesions. *J Nerv Ment Dis* 112:1–45.
- Donoghue JP. 2002. Connecting cortex to machines: recent advances in brain interfaces. *Nat Neurosci* 5(Suppl):1085–8.
- Dubernard JM, Petruzzo P, Lanzetta M, Parmentier H, Martin X, Dawahra M, and others. 2003. Functional results of the first human double-hand transplantation. *Ann Surg* 238:128–36.
- Dum RP, Strick PL. 2002. Motor areas in the frontal lobe of the primate. *Physiol Behav* 77:677–82.
- Dum RP, Strick PL. 2003. An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. *J Neurophysiol* 89:634–9.
- Fagg AH, Arbib MA. 1998. Modeling parietal-premotor interactions in primate control of grasping. *Neural Netw* 11:1277–303.
- Faillenot I, Toni I, Decety J, Gregoire MC, Jeannerod M. 1997. Visual pathways for object-oriented action and object recognition: functional anatomy with PET. *Cereb Cortex* 7:77–85.

- Fogassi L, Gallese V, Buccino G, Craighero L, Fadiga L, Rizzolatti G. 2001. Cortical mechanism for the visual guidance of hand grasping movements in the monkey: a reversible inactivation study. *Brain* 124:571–86.
- Fox PT, Raichle ME. 1986. Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects. *Proc Natl Acad Sci U S A* 83:1140–4.
- Frey SH, Vinton D, Norlund R, Grafton ST. 2005. Cortical topography of human anterior intraparietal cortex active during visually guided grasping. *Brain Res Cogn Brain Res* 23:397–405.
- Gallese V, Murata A, Kaseda M, Niki N, Sakata H. 1994. Deficit of hand preshaping after muscimol injection in monkey parietal cortex. *Neuroreport* 5:1525–9.
- Galletti C, Kutz DF, Gamberini M, Breveglieri R, Fattori P. 2003. Role of the medial parieto-occipital cortex in the control of reaching and grasping movements. *Exp Brain Res* 153:158–70.
- Gardner EP, Babu KS, Reitzen SD, Ghosh S, Brown AS, Chen J, and others. 2007. Neurophysiology of prehension. I. Posterior parietal cortex and object-oriented hand behaviors. *J Neurophysiol* 97:387–406.
- Gardner EP, Debowy DJ, Ro JY, Ghosh S, Srinivasa Babu K. 2002. Sensory monitoring of prehension in the parietal lobe: a study using digital video. *Behav Brain Res* 135:213–24.
- Gibson AR, Horn KM, Van Kan PLE. 1994. Grasping cerebellar functions. In: Castiello UBK, editor. *Insights into the reach to grasp movement*. Amsterdam: Elsevier Science. p 129–50.
- Giraux P, Sirigu A, Schneider F, Dubernard JM. 2001. Cortical reorganization in motor cortex after graft of both hands. *Nat Neurosci* 4:691–2.
- Glover S. 2003. Optic ataxia as a deficit specific to the on-line control of actions. *Neurosci Biobehav Rev* 27:447–56.
- Glover S, Miall RC, Rushworth MFS. 2005. Parietal rTMS disrupts the initiation but not the execution of on-line adjustments to a perturbation of object size. *J Cogn Neurosci* 17:124–36.
- Godschalk M, Lemon RN, Kuypers HG, Ronday HK. 1984. Cortical afferents and efferents of monkey postarcuate area: an anatomical and electrophysiological study. *Exp Brain Res* 56:410–24.
- Godschalk M, Lemon RN, Nijs HG, Kuypers HG. 1981. Behaviour of neurons in monkey peri-arcuate and precentral cortex before and during visually guided arm and hand movements. *Exp Brain Res* 44:113–6.
- Gonzalez CL, Whitwell RL, Morrissey B, Ganel T, Goodale MA. 2007. Left handedness does not extend to visually guided precision grasping. *Exp Brain Res* 182:275–9.
- Grafton ST, Arbib MA, Fadiga L, Rizzolatti G. 1996. Localization of grasp representations in humans by positron emission tomography. 2. Observation compared with imagination. *Exp Brain Res* 112:103–11.
- Grosskopf A, Kuitz-Buschbeck JP. 2006. Grasping with the left and right hand: a kinematic study. *Exp Brain Res* 168:230–40.
- Haggard P, Jenner J, Wing A. 1994. Coordination of aimed movements in a case of unilateral cerebellar damage. *Neuropsychologia* 32:827–46.
- Hoover JE, Strick PL. 1993. Multiple output channels in the basal ganglia. *Science* 259:819–21.
- Hoover JE, Strick PL. 1999. The organization of cerebellar and basal ganglia outputs to primary motor cortex as revealed by retrograde transneuronal transport of herpes simplex virus type 1. *J Neurosci* 19:1446–63.
- Hyvarinen J, Poranen A. 1974. Function of the parietal associative area 7 as revealed from cellular discharges in alert monkeys. *Brain* 97:673–92.
- Iwamura Y, Tanaka M. 1978. Postcentral neurons in hand region of area 2: their possible role in the form discrimination of tactile objects. *Brain Res* 150:662–6.
- Iwamura Y, Tanaka M, Hikosaka O, Sakamoto M. 1995. Postcentral neurons of alert monkeys activated by the contact of the hand with objects other than the monkey's own body. *Neurosci Lett* 186:127–30.
- Iwamura Y, Tanaka M, Sakamoto M, Hikosaka O. 1985. Vertical neuronal arrays in the postcentral gyrus signaling active touch: a receptive field study in the conscious monkey. *Exp Brain Res* 58:412–20.
- Jakobson LS, Archibald Y, Carey D, Goodale MA. 1991. A kinematic analysis of reaching and grasping movements in a patient recovering from optic ataxia. *Neuropsychologia* 29:803–9.
- Jeanerod M. 1986. The formation of finger grip during prehension. A cortically mediated visuomotor pattern. *Behav Brain Res* 19:99–116.
- Jeanerod M, Arbib MA, Rizzolatti G, Sakata H. 1995. Grasping objects—the cortical mechanisms of visuomotor transformation. *Trends Neurosci* 18:314–20.
- Jeanerod M, Decety J, Michel F. 1994. Impairment of grasping movements following a bilateral posterior parietal lesion. *Neuropsychologia* 32:369–80.
- Jones NF. 2002. Concerns about human hand transplantation in the 21st century. *J Hand Surg [Am]* 27:771–87.
- Kalaska JF, Scott SH, Cisek P, Sergio LE. 1997. Cortical control of reaching movements. *Curr Opin Neurobiol* 7:849–59.
- Kim JS. 2001. Predominant involvement of a particular group of fingers due to small, cortical infarction. *Neurology* 56:1677–82.
- Kroliczak G, Cavina-Pratesi C, Goodman DA, Culham JC. 2007. What does the brain do when you fake it? An fMRI study of pantomimed and real grasping. *J Neurophysiol* 97:2410–22.
- Kubota K. 1996. Motor cortical muscimol injection disrupts forelimb movement in freely moving monkeys. *Neuroreport* 7:2379–84.
- Lang CE, Bastian AJ. 1999. Cerebellar subjects show impaired adaptation of anticipatory EMG during catching. *J Neurophysiol* 82:2108–19.
- Lang CE, Schieber MH. 2003. Differential impairment of individuated finger movements in humans after damage to the motor cortex or the corticospinal tract. *J Neurophysiol* 90:1160–70.
- Lang CE, Schieber MH. 2004. Reduced muscle selectivity during individuated finger movements in humans after damage to the motor cortex or corticospinal tract. *J Neurophysiol* 91:1722–33.
- Lassek AM. 1954. Motor deficits produced by posterior rhizotomy versus section of the dorsal funiculus. *Neurology* 4:120–3.
- Latash ML, Yarrow K, Rothwell JC. 2003. Changes in finger coordination and responses to single pulse TMS of motor cortex during practice of a multifinger force production task. *Exp Brain Res* 151:60–71.
- Lawrence DG, Kuypers HG. 1968. The functional organization of the motor system in the monkey. II. The effects of lesions of the descending brain-stem pathways. *Brain* 91:15–36.
- Lemon RN. 1993. The G. L. Brown Prize Lecture. Cortical control of the primate hand. *Exp Physiol* 78:263–301.
- Lemon RN, Johansson RS, Westling G. 1995. Corticospinal control during reach, grasp, and precision lift in man. *J Neurosci* 15:6145–56.
- Li S, Latash ML, Yue GH, Siemionow V, Sahgal V. 2003. The effects of stroke and age on finger interaction in multi-finger force production tasks. *Clin Neurophysiol* 114:1646–55.
- Logothetis NK, Guggenberger H, Peled S, Pauls J. 1999. Functional imaging of the monkey brain. *Nat Neurosci* 2:555–62.
- Logothetis NK, Pauls J, Augath M, Trinath T, Oeltermann A. 2001. Neurophysiological investigation of the basis of the fMRI signal. *Nature* 412:150–7.
- Mason CR, Hendrix CM, Ebner TJ. 2006. Purkinje cells signal hand shape and grasp force during reach-to-grasp in the monkey. *J Neurophysiol* 95:144–58.
- Mason CR, Miller LE, Baker JF, Houk JC. 1998. Organization of reaching and grasping movements in the primate cerebellar nuclei as revealed by focal muscimol inactivations. *J Neurophysiol* 79:537–54.
- Matelli M, Camarda R, Glickstein M, Rizzolatti G. 1986. Afferent and efferent projections of the inferior area 6 in the macaque monkey. *J Comp Neurol* 251:281–98.
- Matelli M, Luppino G. 1996. Thalamic input to mesial and superior area 6 in the macaque monkey. *J Comp Neurol* 372:59–87.
- Matelli M, Luppino G, Rizzolatti G. 1985. Patterns of cytochrome oxidase activity in the frontal agranular cortex of the macaque monkey. *Behav Brain Res* 18:125–36.
- Matelli M, Luppino G, Rizzolatti G. 1991. Architecture of superior and mesial area 6 and the adjacent cingulate cortex in the macaque monkey. *J Comp Neurol* 311:445–62.

- Milner AD, Dijkerman HC, McIntosh RD, Rossetti Y, Pisella L. 2003. Delayed reaching and grasping in patients with optic ataxia. *Prog Brain Res* 142:225–42.
- Milner AD, Dijkerman HC, Pisella L, McIntosh RD, Tilikete C, Vighetto A, and others. 2001. Grasping the past. Delay can improve visuomotor performance. *Curr Biol* 11:1896–901.
- Moll L, Kuypers HG. 1977. Premotor cortical ablations in monkeys: contralateral changes in visually guided reaching behavior. *Science* 198:317–9.
- Mountcastle VB, Lynch JC, Georgopoulos A, Sakata H, Acuna C. 1975. Posterior parietal association cortex of the monkey: command functions for operations within extrapersonal space. *J Neurophysiol* 38:871–908.
- Muakkassa KF, Strick PL. 1979. Frontal lobe inputs to primate motor cortex: evidence for four somatotopically organized 'premotor' areas. *Brain Res* 177:176–82.
- Muir RB, Lemon RN. 1983. Corticospinal neurons with a special role in precision grip. *Brain Res* 261:312–6.
- Murata A, Fadiga L, Fogassi L, Gallese V, Raos V, Rizzolatti G. 1997. Object representation in the ventral premotor cortex (area F5) of the monkey. *J Neurophysiol* 78:2226–30.
- Murata A, Gallese V, Luppino G, Kaseda M, Sakata H. 2000. Selectivity for the shape, size, and orientation of objects for grasping in neurons of monkey parietal area AIP. *J Neurophysiol* 83:2580–601.
- Napier J. 1980. *Hands*. George A, editor. London: Unwin.
- Nelissen K, Luppino G, Vanduffel W, Rizzolatti G, Orban GA. 2005. Observing others: multiple action representation in the frontal lobe. *Science* 310:332–6.
- Pascual-Leone A, Walsh V, Rothwell J. 2000. Transcranial magnetic stimulation in cognitive neuroscience—virtual lesion, chronometry, and functional connectivity. *Curr Opin Neurobiol* 10:232–7.
- Passingham RE. 1987. Two cortical systems for directing movement. *Ciba Found Symp* 132:151–64.
- Ramnani N, Behrens TE, Penny W, Matthews PM. 2004. New approaches for exploring anatomical and functional connectivity in the human brain. *Biol Psychiatry* 56:613–9.
- Rand MK, Shimansky Y, Stelmach GE, Bracha V, Bloedel JR. 2000. Effects of accuracy constraints on reach-to-grasp movements in cerebellar patients. *Exp Brain Res* 135:179–88.
- Raos V, Umiltà MA, Gallese V, Fogassi L. 2004. Functional properties of grasping-related neurons in the dorsal premotor area F2 of the macaque monkey. *J Neurophysiol* 92:1990–2002.
- Rice NJ, Tunik E, Grafton ST. 2006. The anterior intraparietal sulcus mediates grasp execution, independent of requirement to update: new insights from transcranial magnetic stimulation. *J Neurosci* 26:8176–82.
- Rizzolatti G, Camarda R, Fogassi L, Gentilucci M, Luppino G, Matelli M. 1988. Functional organization of inferior area 6 in the macaque monkey. II. Area F5 and the control of distal movements. *Exp Brain Res* 71:491–507.
- Rizzolatti G, Fadiga L, Matelli M, and others. 1996. Localization of grasp representations in humans by PET: 1. Observation versus execution. *Exp Brain Res* 11:246–52.
- Rizzolatti G, Luppino G. 2001. The cortical motor system. *Neuron* 31:889–901.
- Rizzolatti G, Luppino G, Matelli M. 1998. The organization of the cortical motor system: new concepts. *Electroencephalogr Clin Neurophysiol* 106:283–96.
- Rossetti Y, Pisella L, Vighetto A. 2003. Optic ataxia revisited: visually guided action versus immediate visuomotor control. *Exp Brain Res* 153:171–9.
- Sakata H, Kusunoki M. 1992. Organization of space perception: neural representation of three-dimensional space in the posterior parietal cortex. *Curr Opin Neurobiol* 2:170–4.
- Sakata H, Taira M, Murata A, Mine S. 1995. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cereb Cortex* 5:429–38.
- Schettino LF, Adamovich SV, Hening W, Tunik E, Sage J, Poizner H. 2006. Hand reshaping in Parkinson's disease: effects of visual feedback and medication state. *Exp Brain Res* 168:186–202.
- Schieber MH. 1999. Somatotopic gradients in the distributed organization of the human primary motor cortex hand area: evidence from small infarcts. *Exp Brain Res* 128:139–48.
- Schieber MH, Poliakov AV. 1998. Partial inactivation of the primary motor cortex hand area: effects on individuated finger movements. *J Neurosci* 18:9038–54.
- Schieber MH, Santello M. 2004. Hand function: peripheral and central constraints on performance. *J Appl Physiol* 96:2293–300.
- Smith AM, Dugas C, Fortier P, Kalaska J, Picard N. 1993. Comparing cerebellar and motor cortical activity in reaching and grasping. *Can J Neurol Sci* 20(Suppl 3):S53–61.
- Taira M, Mine S, Georgopoulos AP, Murata A, Sakata H. 1990. Parietal cortex neurons of the monkey related to the visual guidance of hand movement. *Exp Brain Res* 83:29–36.
- Tallis R. 2004. *The hand. A philosophical enquiry into human being*. Edinburgh (UK): Edinburgh University Press.
- Taylor DM, Tillery SI, Schwartz AB. 2002. Direct cortical control of 3D neuroprosthetic devices. *Science* 296:1829–32.
- Timmann D, Citron R, Watts S, Hore J. 2001. Increased variability in finger position occurs throughout overarm throws made by cerebellar and unskilled subjects. *J Neurophysiol* 86:2690–702.
- Timmann D, Watts S, Hore J. 1999. Failure of cerebellar patients to time finger opening precisely causes ball high-low inaccuracy in overarm throws. *J Neurophysiol* 82:103–14.
- Tipper SP, Howard LA, Houghton G. 1998. Action-based mechanisms of attention. *Philos Trans R Soc Lond B Biol Sci* 353:1385–93.
- Tunik E, Frey SH, Grafton ST. 2005. Virtual lesions of the anterior intraparietal area disrupt goal-dependent on-line adjustments of grasp. *Nat Neurosci* 8:505–11.
- Tunik E, Rice NJ, Hamilton A, Grafton ST. 2007. Beyond grasping: representation of action in human anterior intraparietal sulcus. *Neuroimage* 36:T77–86.
- Twitchell TE. 1951. The restoration of motor function following hemiplegia in man. *Brain* 74:443–80.
- Umiltà MA, Brochier T, Spinks RL, Lemon RN. 2007. Simultaneous recording of macaque premotor and primary motor cortex neuronal populations reveals different functional contributions to visuomotor grasp. *J Neurophysiol* 98:488–501.
- Valero-Cuevas FJ, Hentz VR. 2002. Releasing the A3 pulley and leaving flexor superficialis intact increases pinch force following the Zancolli lasso procedures to prevent claw deformity in the intrinsic palsied finger. *J Orthop Res* 20:902–9.
- van Kan PL, Horn KM, Gibson AR. 1994. The importance of hand use to discharge of interpositus neurons of the monkey. *J Physiol* 480:171–90.
- Wannier T, Bastiaanse C, Colombo G, Dietz V. 2001. Arm to leg coordination in humans during walking, creeping and swimming activities. *Exp Brain Res* 141:375–9.
- Weinrich M, Wise SP. 1982. The premotor cortex of the monkey. *J Neurosci* 2:1329–45.
- Weiss P, Stelmach GE, Hefter H. 1997. Programming of a movement sequence in Parkinson's disease. *Brain* 120:91–102.
- Wenger KK, Musch KL, Mink JW. 1999. Impaired reaching and grasping after focal inactivation of globus pallidus pars interna in the monkey. *J Neurophysiol* 82:2049–60.
- Wise SP, Boussaoud D, Johnson PB, Caminiti R. 1997. Premotor and parietal cortex: corticocortical connectivity and combinatorial computations. *Annu Rev Neurosci* 20:25–42.
- Zackowski KM, Thach WT Jr, Bastian AJ. 2002. Cerebellar subjects show impaired coupling of reach and grasp movements. *Exp Brain Res* 146:511–22.