

THE NEUROSCIENCE OF GRASPING

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Abstract | 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. We reach for objects, grasp and lift them, manipulate them and use them to act on other objects. This review examines one of these actions — grasping. Recent research in behavioural neuroscience, neuroimaging and electrophysiology has the potential to reveal where in the brain the process of grasping is organized, but has yet to address several questions about the sensorimotor transformations that relate to the control of the hands.

PRECISION GRIP

Precision grip is characterized by opposition of the thumb to one or more of the other fingers.

POWER GRIP

In power grip, the fingers are flexed to form a clamp against the palm.

KINEMATICS

Kinematics consider movement in terms of position and displacement (angular and linear) of body segments, centre of gravity, and acceleration and velocities of the whole body or segments of the body.

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Since the origins of neuroscience, hand movements have been the focus of interest of many researchers. In the nineteenth century, the Earl of Bridgewater left UK£7,000 to the Royal Society (UK) for the purpose of sponsoring several treatises. One of these famous treatises — *The Hand*, by Sir Charles Bell¹ — was a remarkable study of the adaptation of human and animal hands. Bell's analyses of the behavioural consequences of anatomical variation and his insights into the relationship between hand and brain function set the stage for modern studies on the structure and grasping functions of the hand.

The study of grasping was advanced by Napier's landmark work on PRECISION and POWER GRIPS^{2–4} (FIG. 1a,b). Napier established that manipulative hand movements were choreographed to achieve a continuous and integrated solution to the biomechanical and neurophysiological constraints of any movement. His model went far beyond showing the physical rationality of these movements — he showed that despite the enormous variability in aspects of movement such as force, posture, duration and speed, the underlying control principles were amazingly elegant. These principles were based on the supposition that the intended activity determines what type of grip is used for any given action (for example, grasping a pen to write involves a different grip from grasping it to put it in a box).

Since these early studies, grasping has been widely investigated in humans and monkeys using various tasks and techniques^{5–7}. These studies aim to integrate information from various domains to ascertain which neural circuits underlie grasping. Here, I

summarize the current state of knowledge on the elaborate mechanisms that facilitate the formation of grip patterns in human and non-human primates. First, I describe the KINEMATICS of grasping in humans and macaque monkeys. Next, I present evidence that grasping requires several neural mechanisms, some of which are concerned with individual finger force and movement, and others that involve a specialized visuomotor system that encodes object features and generates the corresponding hand configurations. Evidence from lesion and neuroimaging studies in humans is compared with neurophysiological studies in monkeys. Although much of the work on grasping comes from monkeys, and this work has contributed to our understanding, caution is necessary when drawing homologies across species. Finally, I highlight factors that, I believe, should be taken into account by neuroscientists in the quest to understand the neural bases of grasping.

The kinematics of grasping

The mechanics of grasping in humans and macaques vary depending on object attributes. Although the substantial differences in hand morphology between these two species are the focus of current debate^{8–10}, it is important to compare grasping in humans and monkeys because of the common practice of looking for homologies between the two species' brains.

Jeannerod^{11,12} coded grasping in terms of changes in grip aperture — the separation between the thumb and the index finger. During a reach-to-grasp movement, there is first a progressive opening of the grip,

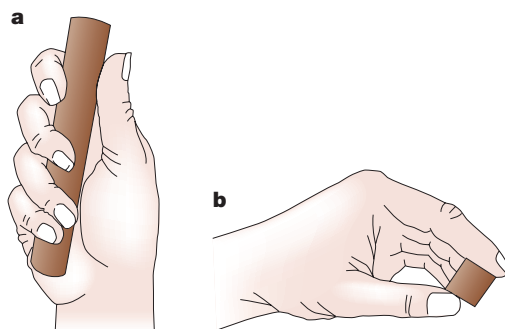


Figure 1 | **Examples of different grasps.** **a** | Power grip between thumb and all fingers. **b** | Precision grip between index finger and thumb. Modified, with permission, from REF. 10 © (1994) Elsevier Science.

with straightening of the fingers, followed by a gradual closure of the grip until it matches the object's size (FIG. 2a). The point in time at which the thumb–finger opening is the largest (maximum grip aperture) is a clearly identifiable landmark that occurs within 60–70% of the duration of the reach and is highly correlated with the size of the object (FIG. 2b,c).

These observations^{11,12} led to a surge in research on human prehension, some of it looking at the relationship between object size and grasping parameters^{13–22}, but much of it dedicated to the investigation of other properties, including fragility²³, size of the contact surface²⁴, texture²⁵ and weight^{26–28}. As recently reviewed²², all these factors influence the kinematics of grasping. Object weight constrains the positioning of the fingers — heavier objects need to be grasped more accurately and with a larger grip than lighter objects²². Grasping slippery objects requires a larger approach parameter, leading to a larger grip earlier in the movement compared with grasping rough-surfaced objects²². So far, such studies have paid little attention to differences in the shape assumed by individual fingers when performing grasping movements to objects. In most cases, only the maximum distance between index finger and thumb was measured and participants were explicitly requested to use a precision grip with no regard given to the size or shape of the object. Therefore, they might not provide valid tests of the extent to which different types of grasping pattern are matched with the shape of the target object.

A fundamental issue that any model of grasping must address is that objects can be grasped in several different ways, with the chosen grip depending on the object's visual properties. A valid investigation of grasping requires us to ask how the motions of individual finger joints are coordinated to produce a particular hand shape^{29–38}. In one series of studies^{30–32}, the information transmitted by hand posture about object shape increased gradually and monotonically as the hand approached the object, reaching a maximum at the time the object was in the grasp of the hand. Importantly, when the maximum aperture of the hand was reached, hand posture had only partially

moulded to the object's contours. It can therefore be questioned whether the maximum distance between the index finger and thumb represents the key kinematic landmark or just a preliminary 'sketch' of the grasping movement.

Although the hand is sensitive to the features of the object that is to be grasped, it is also a skilful motor device that can manipulate objects to achieve a desired goal. The tactile system seems to be important for these pragmatic considerations^{39–42}. Cutaneous receptors in the hand provide information about the action of the hand, including its kinematics and posture, as well as the grip forces and load forces that are used during grasping and manipulation of objects^{39–41}.

Compared with human grasping, little is known about the kinematic characteristics of grasping movements in monkeys^{35,43–45}. Films of a rhesus monkey grasping small pieces of food showed a similar opening of the grip followed by closure before contact with the object as occurs in humans⁴⁴. In addition, the maximum grip aperture for different objects was correlated with object size^{43,44} (FIG. 3). However, these observations were based only on a limited grasping repertoire (the precision grip) and related only to the 'size' effect^{43–45}.

A more recent study³⁵ investigated the monkey's ability to conform its hand configurations to object shape. As in humans, the monkeys used a specific hand shape for each object rather than using a default shape or simply opening and closing the hand around the object. Another similarity to human control of hand shaping was that hand shape began to reflect the geometry of the object to be grasped throughout the reach, attaining a perfect match with object geometry on contact with the object^{30–32}. Nevertheless, only two monkeys were tested and hand-shaping preferences varied across objects and between monkeys when they grasped the same object. For example, one monkey used a precision grip only for one object but preferred to use a palm/finger opposition for all remaining objects. The other monkey preferred to use either a precision or power grasp with its thumb in opposition to the fingers.

Although these experiments indicate that some features of grasping movements are common to macaques and humans, a direct comparison of the two species was not made, which would have taken into account morphological and behavioural differences^{3,4,9,10}. In a study that partly addressed these issues⁴⁵, five macaques were allowed to assume their preferred postural position. The kinematics of grasping a raisin or peanut using a precision grip were compared among these macaques and five humans. To produce conditions similar to those in the macaques, human participants were asked to initiate the task with the hand at the mouth and then to grasp and bring to the mouth a single food item. The angular velocity and acceleration of the finger aperture were significantly higher in macaques than in humans, and macaques made smaller shoulder excursions than humans during the grasping movement. However, despite these differences, some of the general kinematic relationships documented in humans remained in the monkeys.

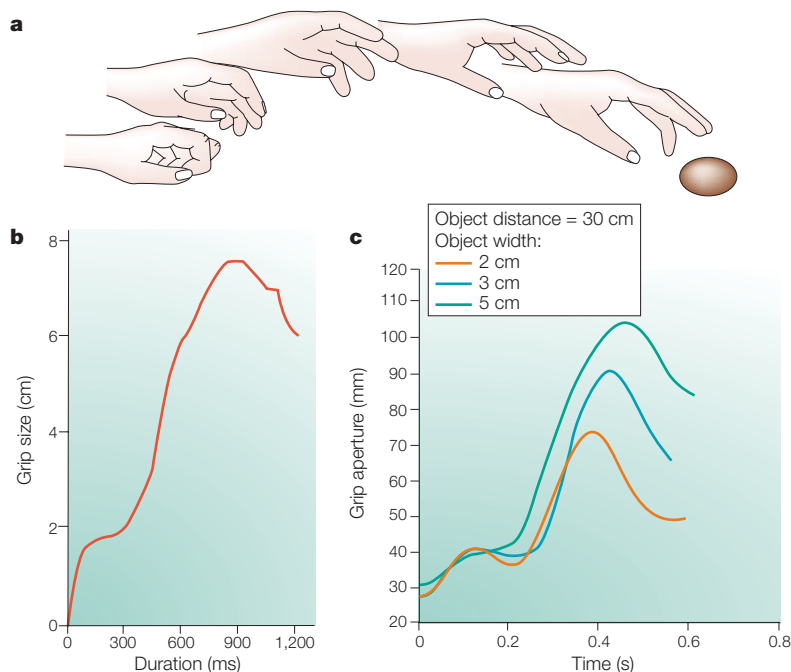


Figure 2 | Kinematics of grasping. **a** | The hand preshapes during its journey to the target object. **b** | Maximal grip aperture (distance between the tip of thumb and the tip of index finger) typically occurs within 70% of movement completion. **c** | Representation of traces demonstrating the scaling of maximum grip aperture with respect to object size. Panels **a** and **b** modified, with permission, from REF. 12 © (1984) Heldref Publications. Panel **c** modified, with permission, from REF. 13 © (1991) Springer.

Researchers have often presumed that the human brain contains homologues of areas in the macaque brain that are involved in grasping. Although there do seem to be homologues of some such areas, for others their existence is less clear. Furthermore, the behavioural differences between species and the methodological differences between studies impel us to treat these homologues with scepticism. Next, I compare the brain areas that are involved in grasping in monkeys and humans (FIG. 4). I then provide suggestions for a more careful and controlled comparison across species.

The neurophysiology of grasping

This section reviews the study of single cells in the monkey brain. Three specific areas relating to grasping have been identified in the monkey cortex — the primary motor cortex (F1), the premotor cortex (PML/F5) and the anterior intraparietal sulcus (AIP) (FIG. 4a). In terms of neural mechanisms, performing a successful grasping action depends primarily on the integrity of the primary motor cortex (F1). In monkeys, lesions of this area produce a profound deficit in the control of individual fingers and consequently disrupt normal grasping^{46–48}.

Information from the primary motor cortex is conveyed to cells in the spinal cord via the corticospinal tract, a primary neural substrate for independent finger movements^{49–51}. Lesioning the corticospinal tract impairs independent finger movements in adult animals⁴⁹. By contrast, such a lesion does not impede

synergistic finger flexion during a power grip⁴⁹. There is also physiological evidence that cortical motor neurons might be relatively more active during independent finger movements than during a power grip. In monkeys, large cortical motor neurons that project to the intrinsic hand muscles are active during the application of low levels of finely controlled force (for example, during a precision grip), but can become paradoxically inactive during a power grip⁴⁹.

The information sent to the spinal cord from the primary motor cortex is also conveyed to the intermediate zone of the cerebellum. Consequently, it has been proposed that the intermediate cerebellum has a specific role in the control of hand movements during grasping^{52–54}. This hypothesis has been tested in studies in which monkeys were trained to make two types of reaching movement. One movement consisted of reaching out while the hand gripped the handle of a device; the other comprised reaching out to grasp a raisin. The idea behind this experiment was that if the intermediate cerebellum is especially important for grasping, only reaching out to grasp a raisin should elicit discharge modulation in this area. The results were clear: 93% of cells recorded from the output nucleus of the intermediate cerebellum (the interpositus nucleus) were more active during reaching out to grasp than when the hand simply gripped the handle⁵².

Another fundamental process for a successful grasp involves a transformation of the intrinsic properties of the object, visually described, into motor actions⁵⁵. Two key cortical areas seem to be involved in visuomotor transformations for grasping in monkeys: area F5 and the AIP. Area F5 forms the rostral part of the monkey ventral PMC and consists of two main sectors: one on the posterior bank of the inferior arcuate sulcus (F5ab), the other on the dorsal convexity (F5c). The AIP is a small zone in the rostral part of the posterior bank of the intraparietal sulcus that is directly connected to area F5ab^{56–59} (FIG. 4a).

In monkeys that have been trained to grasp various objects, the activities of AIP and F5 neurons show striking similarities and important differences^{60–67} (FIG. 5). For example, AIP and F5 neurons code for grasping actions that relate to the type of object to be grasped (for example, precision grip)^{64,65}. However, AIP neurons seem to represent the entire action, whereas F5 neurons seem to be concerned with a particular segment of the action^{63,64}. Another important difference is that visual responses to three-dimensional objects are found more frequently in AIP than in F5 (REF. 64). This indicates that AIP, although part of a parieto-frontal circuit that is dedicated to hand movements, contains a population of neurons that code three-dimensional objects in visual terms.

On the basis of the functional roles of neurons in areas AIP and F5, Fagg and Arbib⁶⁸ have developed a model in which area AIP provides multiple descriptions of three-dimensional objects for the purpose of manipulation, whereas area F5 is mainly involved in selecting the most appropriate motor prototype from a MOTOR VOCABULARY⁶⁰, for example, the type of grip that is effective in interacting with a target object. Confirmation

MOTOR VOCABULARY
The motor vocabulary comprises ‘words’, each of which is represented by a population of F5 neurons. These words select specific ‘motor prototypes’, such as the configuration of fingers that is necessary for the precision grasp.

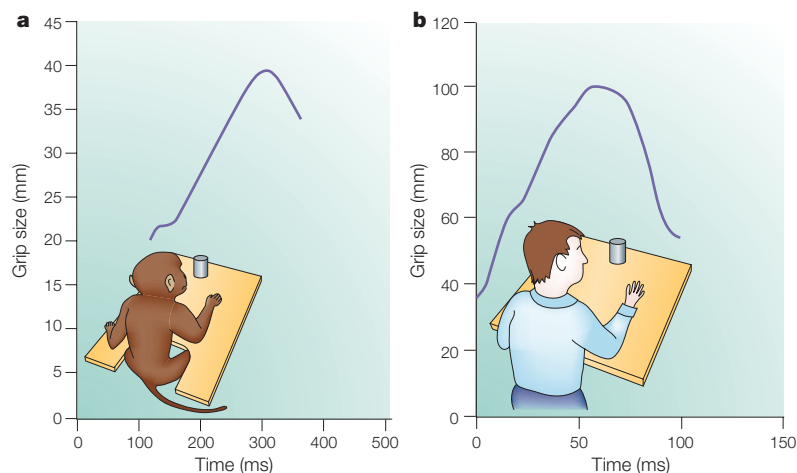


Figure 3 | Comparison of the kinematics of grasping in monkeys and humans: effect of size. Grip size in (a) a macaque monkey and (b) a human subject. In both species, the grasping component is characterized by a grip size that increases up to a maximum and then decreases towards the end of the movement. The macaque data are presented in absolute time, whereas those for the human participants are presented in normalized time, as a percentage of movement duration. The object diameter was 15 mm. Modified, with permission, from REF. 44 © (2000) Elsevier Science.

that the AIP–F5 circuit is likely to be relevant for grasping comes from reversible, independent inactivation of each of these areas in the monkey^{69–71}. Inactivation of either AIP or F5 markedly impaired hand shaping during reaching, and the hand posture after inactivation was inappropriate for the object's size and shape.

Like vision, somesthesia is a crucial source of information for the motor system. Somatic receptors in muscles, joints and skin provide information regarding the current posture of the hand and its location and orientation with respect to potential targets for grasping. This information is necessary to compute a trajectory to bring the hand to the object and grasp it properly.

To investigate the conjunction of visual and somatic processing, one study compared the timing of spike trains recorded by single-unit recording in the somatosensory cortex (SI) and the AIP cortex of the same animals during a reach-to-grasp task⁷². Importantly, kinematics were also recorded during the task to define the stages of the reach-to-grasp movement. The response of cells in AIP was influenced by the shape of the target object. Neurons in SI typically responded later than those in AIP, showing a significant increase in firing rates only after the hand touched the object, and peaking when grasping was secure. SI neurons rarely differentiated the shape of the grasped object in the manner that occurred in AIP neurons.

Given the wealth of evidence for a grasping circuit involving several areas in the monkey brain, the natural question is whether a similar circuit exists in humans. For ethical reasons, invasive physiological recording of brain activity is rarely possible in humans. Nonetheless, considerable progress has been made towards understanding the neural substrates of grasping in humans, mainly from studies of patients with brain damage and neuroimaging experiments.

The neuropsychology of grasping

Evidence that the human brain contains specialized circuits for grasping comes mainly from the neuropsychological literature. To facilitate comparison between humans and monkeys, I discuss brain areas in the sequence used above: primary motor cortex, PMC and posterior parietal cortex (PPC).

As in the monkey, lesions of the human primary motor cortex or corticospinal fibres profoundly disrupt grasping^{73–75}. Such lesions typically lead to grasping movements that are initially characterized by the loss of independent finger movement, although synergistic movements of all fingers (a power grip) remain intact. Independent finger movements sometimes recover later.

No grasping studies have yet been carried out on patients with lesions of the ventral PMC. However, there is some evidence that the AIP has a specific role in grasping in humans. Binkofski and colleagues⁷⁶ localized the area responsible for grasping in humans to the AIP, contralateral to the impaired hand. In line with the results obtained from monkeys in which AIP has been inactivated, human patients with AIP lesions had deficits in grasping, whereas reaching remained relatively intact.

Striking evidence for a deficit in visually guided grasping has come from patients with optic ataxia^{77,78}. 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). Jeannerod⁷⁹ found that in reaching out 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). Subsequently, various patients have been described that show specific deficits in the control of grasping after damage to the SPL. Patient V.K.⁸⁰, for example, showed an apparently normal early phase of hand opening during attempts to grasp an object, but her on-line control of grip aperture quickly degenerated, resulting in numerous secondary peaks in the grip aperture profile (FIG. 6c), rather than a single peak, which is typical of a healthy subject. Patient I.G.^{81,82} also showed considerable deficits in the scaling of her maximum grip aperture to the size of an object. Another patient, A.T.⁸³, who had 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 a 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. So, for commonly used objects, cognitive cues and previous knowledge can be used to determine the size of the object. This indicates that the meaning attached to an object might modulate classic grasping circuits. This issue will be discussed again in the 'Future directions' section.

It is difficult to integrate these grasping deficits in humans after lesions of the SPL with the results of neurophysiological work in monkeys. First, in monkeys, the

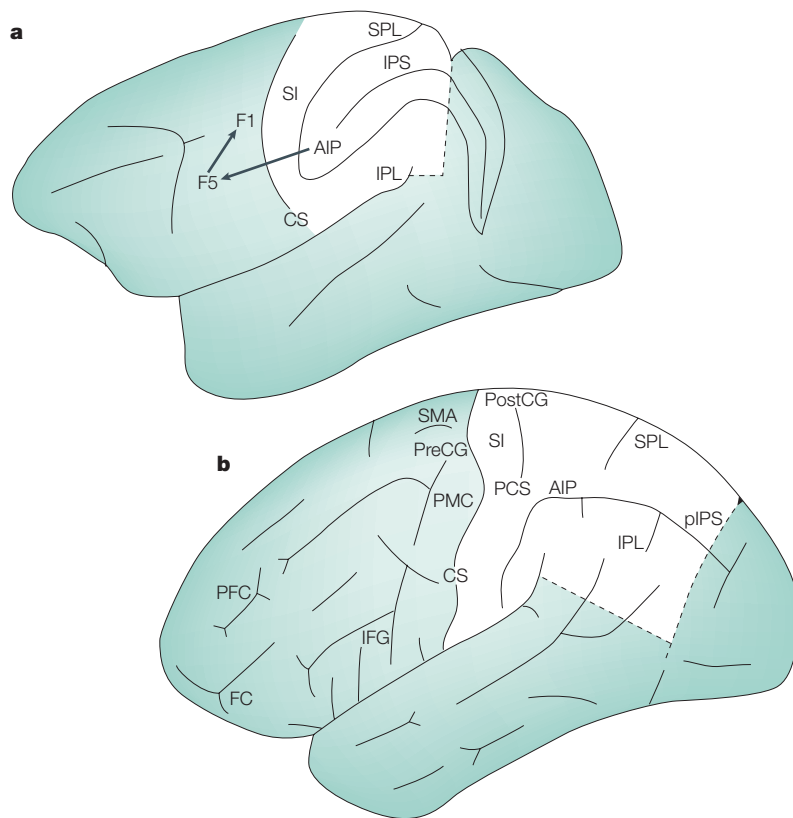


Figure 4 | Comparison between neural circuits for grasping in macaque monkeys and humans. Lateral view of the monkey and human cerebral cortex. **a** | For the monkey, the visuomotor stream for grasping (AIP–F5) and the stream from F5 to F1 are indicated by large arrows. **b** | Grasping areas in humans, as identified by neuroimaging studies. Cortical areas that control grasping are also connected with basal ganglia and cerebellar circuits. These circuits, although involved in grasping, are not shown in the figure. AIP, anterior intraparietal area; CS, central sulcus; FC, frontal cortex; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; IPS, intraparietal sulcus; PCS, postcentral sulcus; PFC, prefrontal cortex; pIPS, posterior intraparietal sulcus; PMC, premotor cortex; PostCG, postcentral gyrus; PreCG, precentral gyrus; SI, primary somatosensory cortex; SMA, supplementary motor area; SPL, superior parietal lobule. Modified, with permission, from REF. 101 © (2001) Elsevier Science.

SPL seems to be principally related to the elaboration of somatosensory rather than visuomotor information⁶⁷. Second, although in monkeys some parts of the SPL do receive visual information, these areas seem to be mainly concerned with reaching rather than grasping⁸⁴. Furthermore, there is reason to believe that, owing to the relative expansion of the parietal lobes in humans relative to monkeys, the human SPL might be the homologue of the monkey IPL, although this is still under debate⁸⁵.

Although there is some evidence that supports homologies between the neural correlates of grasping in monkeys and humans, the nature of these homologies is still unclear and controversial. Studies of patients have provided some details about how the kinematics of grasping are compromised after brain lesions. Importantly, these observations could be linked with those obtained from neurophysiological studies, in which the cortical mechanisms for the visual guidance of hand grasping have been inactivated^{69,70}. However, the lack of quantitative measures of grasping kinematics

during these experiments does not allow us to make direct comparisons of behavioural and neural data between species. Brain scanning procedures that provide images of normal brain function might assist such comparisons between species, by measuring activation patterns in different cortical areas when healthy humans perform grasping tasks.

The neuroimaging of grasping

Brain imaging experiments have investigated the existence and localization in humans of cortical circuits for grasping similar to those in monkeys. In these experiments, subjects have been scanned during either reach-to-grasp actions or only grasping actions using the (dominant) right hand. Some studies using functional MRI (fMRI) have focused on selected neuroanatomical REGIONS OF INTEREST (ROI), principally the presumed human homologue of monkey AIP. Other studies, using positron emission tomography (PET) to examine activity in the entire brain, have found activation associated with visually guided grasping in many more areas (FIG. 4b).

Early attempts to use brain imaging to identify the functional anatomy underlying the generation of goal-directed arm movements during the action of reaching and grasping movements in humans used PET⁸⁶. However, the results of PET studies are difficult to integrate, given radical differences in experimental conditions and set ups: below they are grouped in terms of design similarities.

When participants were asked to reach and grasp illuminated cylindrical objects or to point to the same targets with their right hand, increases in regional cerebral blood flow (rCBF) (compared with looking at the target) were found in many cortical and subcortical areas, including the contralateral motor cortex, PMC, ventral supplementary motor area, cingulate cortex, SPL, dorsal occipital cortex and left parietal operculum⁸⁷. In another study⁸⁸, subjects were asked to touch or grasp one of five cylinders with their right hand. Compared with touching, grasping increased rCBF in extensive regions of the bilateral PMC, the PPC and the prefrontal cortex (PFC).

Another study⁸⁹ did not include a control view condition; rather, it used ‘grasping’, ‘pointing’ and ‘matching’ conditions. In the matching condition, subjects compared the shape of the presented object with that of the previous one. Whereas the comparison between grasping and pointing showed an increased rCBF in the anterior part of the PPC, the comparison between grasping and matching showed an increased rCBF in the cerebellum, the left frontal cortex around the central sulcus, the medial frontal cortex and the left IPL.

In a study by Rizzolatti *et al.*⁹⁰, participants were tested in a ‘grasping’ condition that was compared with two ‘observation’ conditions. In one observation condition, participants observed grasping movements of common objects performed by the experimenter. In the other, they looked at the object. Grasping with the right hand significantly activated the left supramotor cortical areas, the left SPL, the cuneus bilaterally, the left putamen and the cerebellum bilaterally.

REGIONS OF INTEREST (ROI). A type of neuroimaging analysis in which specific areas rather than the entire brain are targeted and analysed.

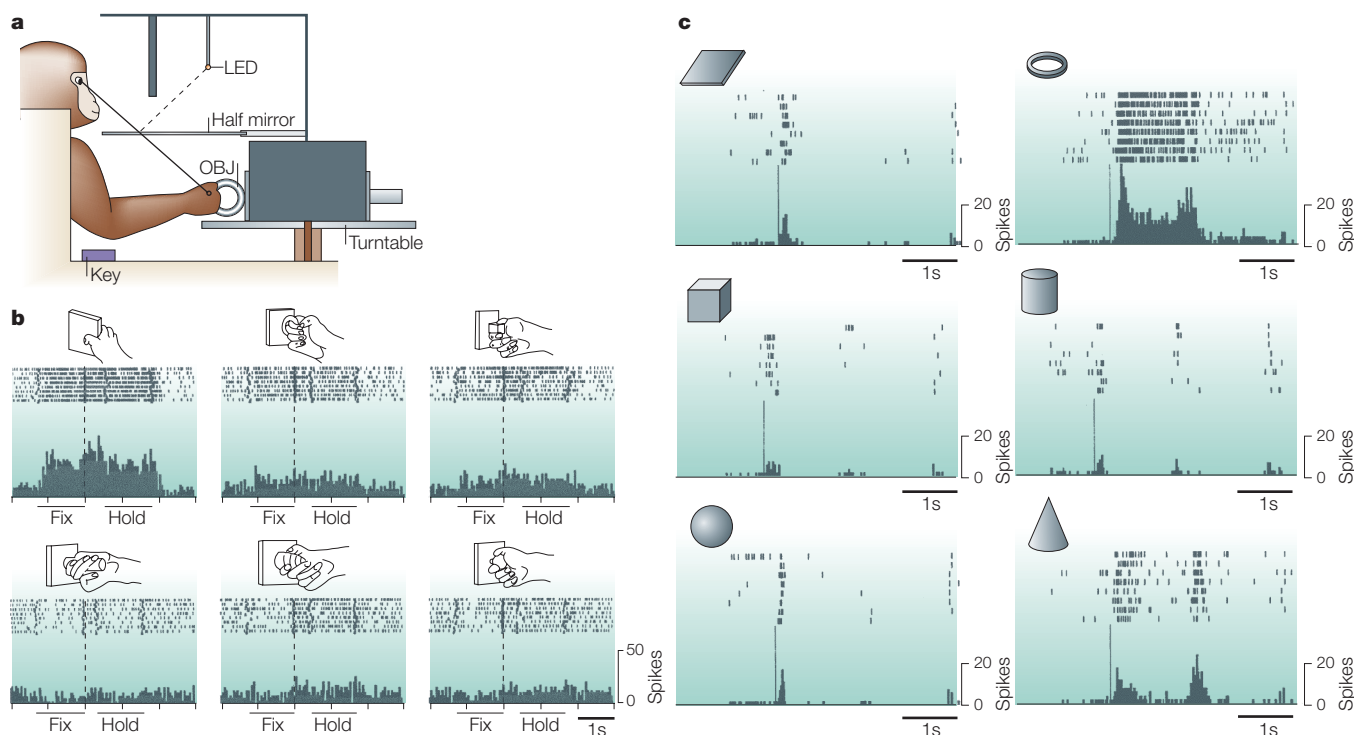


Figure 5 | Types of neuron in monkey anterior intraparietal area and F5 that are involved in hand manipulation.

a | Experimental setup. The monkey was seated in front of a box, which housed six different objects (OBJ). Objects were 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) was projected onto the object and the monkey was required to fixate it and press a key. Key pressing turned on the light inside the box and made the object visible. After the monkey pressed the key for 1.0–1.2 s, the LED changed colour (green, go signal) and the monkey was allowed to release the lever and grasp the object. **b** | Highly selective activity of an object-type visuomotor anterior intraparietal area (AIP) neuron for six different objects. Each of the raster and histograms shows the activity levels during the manipulation of medium-sized objects. The illustration above each raster indicates the objects and the type of handgrip. **c** | Activity of F5 neurons during observation and grasping of objects similar to those used for AIP neurons. In panels **b** and **c**, rasters and histograms are aligned with the go signal (the moment the object becomes visible), which are represented by broken and solid lines in panels **b** and **c**, respectively. Panels **a** and **b** modified, with permission, from REF. 64 © (2000) American Physiological Society; panel **c** modified, with permission, from REF. 109 © (2001) Cell Press.

Another study⁹¹ compared three conditions: a precision grip action towards a sweet with the right hand, grasping with the mouth and observing the sweet. The results showed an extensive hand grasping network, including the left precentral and postcentral gyri (preCG and postCG, respectively), along the midline in the cingulate gyrus, the precuneus and the IPL bilaterally.

In the above studies, little attention was given to possible differential activations when performing different types of grasping action. Rather, participants typically used only a precision grip. A natural question might be whether having to select and execute a particular type of grasp would recruit different brain areas from those that would be recruited simply by repeating the same type of grasp throughout the experiment.

To address this issue, Grafton and colleagues⁹² asked subjects to perform three tasks requiring specific grasping actions with the right hand. For the power task, participants performed only power grips, using the whole hand. For the precision task, participants performed only a precision grip, using the thumb and index finger. For the conditional task, participants performed either a power grip or a precision grip, depending on the

colour of a cue. Finally, there was a rest task in which participants held their arm stationary in a power grip. The results suggest that grasp selection activated the preCG, the postCG and two sites in the parietal cortex — the SPL and AIP.

The PET studies reviewed above provide some support for homology between grasping circuits in humans and monkeys. However, many areas were activated that have not been linked with grasping in monkeys and the results are inconsistent. There are several possible reasons for these mixed results: the relatively low spatial and temporal resolution of PET; the possible presence of motion artefacts, which are particularly problematic in motor control experiments; the lack of experimental control for somatosensory finger stimulation that co-occurs with grasping in some studies; and the varying experimental protocols.

The development of fMRI has coincided with improvements in design to help address many of the problems of PET studies. fMRI provides superior spatial resolution to PET imaging, and studies using fMRI have been improved to eliminate many of the possible confounding variables seen in the earlier PET studies.

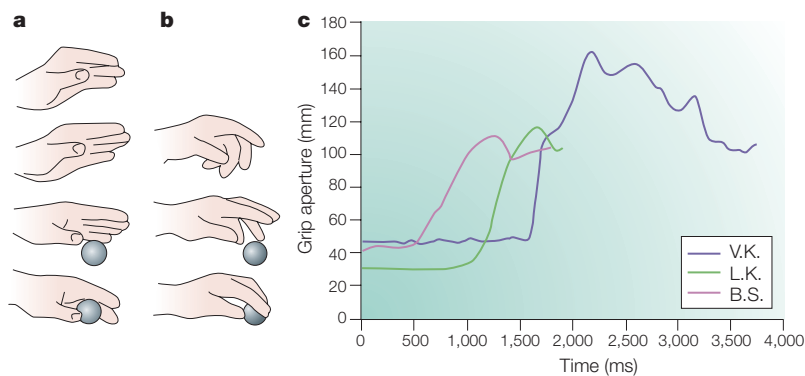


Figure 6 | Grip aperture profiles of patients with brain damage. Comparison of the pattern of finger grip in a patient, 'Biz', with optic ataxia during reaching with the affected hand (a) and the normal hand (b). c | Comparison of the abnormal pattern of finger grip in a patient, V.K., with the pattern of finger grip of two neurologically healthy participants (L.K. and B.S.). Panels a and b modified, with permission, from REF. 79 © (1986) Elsevier Science. Panel c modified, with permission, from REF. 80 © (1991) Elsevier Science.

One study⁷⁶ used an alternating task design, in which grasping of a rectangular object, the orientation of which could vary, was used as the activation condition and pointing towards the object was used as the baseline condition: the subjects presumably used a precision grip. The results showed a specific activation of the lateral bank of AIP in grasping tasks, together with activations, including the contralateral sensorimotor cortex, bilateral PMC and the PPC. The activated part of AIP is the same area in which lesions in humans and chemical deactivation in monkeys lead to grasping deficits.

This result was further confirmed by studies that used an ROI approach and an event-related design^{93–96}. For example, subjects were presented with a diverse and unpredictable sequence of objects (rectangular shapes of varied length and orientation) using custom equipment termed 'the grasparatus' (FIG. 7a), and had to reach towards the long axis of the objects and grasp them using a precision grip. The results provided strong evidence that AIP contributes to the ability to execute grasping actions towards objects (FIG. 7b). Unfortunately, the fact that subjects were constrained to a single type of grasp prevented a more complete comparison with the monkey AIP, which contains selective motor-dominant neurons that represent various patterns of hand movements appropriate to grasping particular objects. In this respect, brain activity recorded in 14 subjects who were trained to reach and grasp an object either with a precision grip or with whole-hand prehension (FIG. 7c) (C. Begliomini, M. Wall, A. T. Smith and U.C., unpublished observations) showed that AIP was active exclusively for the precision grip task (FIG. 7d), and did not show any activity during the whole-hand grasp (FIG. 7e). The left preCG and postCG were active for both types of grasp. These findings indicate that, in humans, AIP might be specifically tuned for precision grips.

Grezes and colleagues⁹⁷ looked for a similar neural network for grasping in the human brain to those in area F5 of macaques. In three execution conditions,

subjects executed a type of grasp that was: appropriate for the object that they viewed; imitated a pantomime action they viewed; or imitated a viewed hand grasping an object. In the baseline condition, subjects executed a power grip on all trials while viewing a stationary background. One of the objects used was a large object that would normally be grasped with a power grip; the other was small and would normally be grasped by a precision grip. The areas that were activated were consistent with the monkey AIP–F5 visuomotor circuit. The results showed activation of the AIP, the inferior frontal gyrus and the PMC during grasping movements. Unfortunately, the data were not analysed separately for the two types of grasp and the action was confined to the grasping component, as participants did not perform overt arm movements.

By contrast, no AIP activation was found in a study⁹⁸ in which participants performed a reach-to-grasp action (a precision grip) towards an object that could appear at any one of three locations. Activations related to grasping were found in SPL, the posterior intraparietal sulcus and PMC, as well as in various subcortical areas, including the cerebellum and thalamus.

Other issues involved in grasping relate to force production for specific grasping patterns^{99,100}. Ehrson and colleagues^{99,100} compared human brain activity during a precision grip and a power grip. The activity recorded in the contralateral primary sensorimotor cortex was higher during a power grip than a precision grip. By contrast, the activity in the ventral PMC, the rostral cingulate motor area and at several locations in the PPC and the PFC was stronger during the precision grip than the power grip. The power grip was associated predominantly with contralateral activity, whereas the precision grip task involved extensive activation in both hemispheres. These findings indicate that, in addition to the primary motor cortex, premotor and parietal areas are important for control of fingertip forces during precision grip.

The human brain regions that are activated during grasping include components of the circuit that has been identified by neurophysiological studies of the macaque brain, including primary motor, premotor and AIP areas. However, many other areas also seem to be involved, including prefrontal, superior parietal, primary somatosensory, cerebellar and subcortical areas. In PET and fMRI studies, there are inconsistencies in the experimental models, indicating the need for further and more controlled experiments.

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, we must question the extent to which it is possible to identify in humans a neural circuit for grasping that is similar to that in monkeys. At a behavioural level, the suggested homology should be taken with caution. There are clear behavioural and morphological differences that make a direct comparison between the

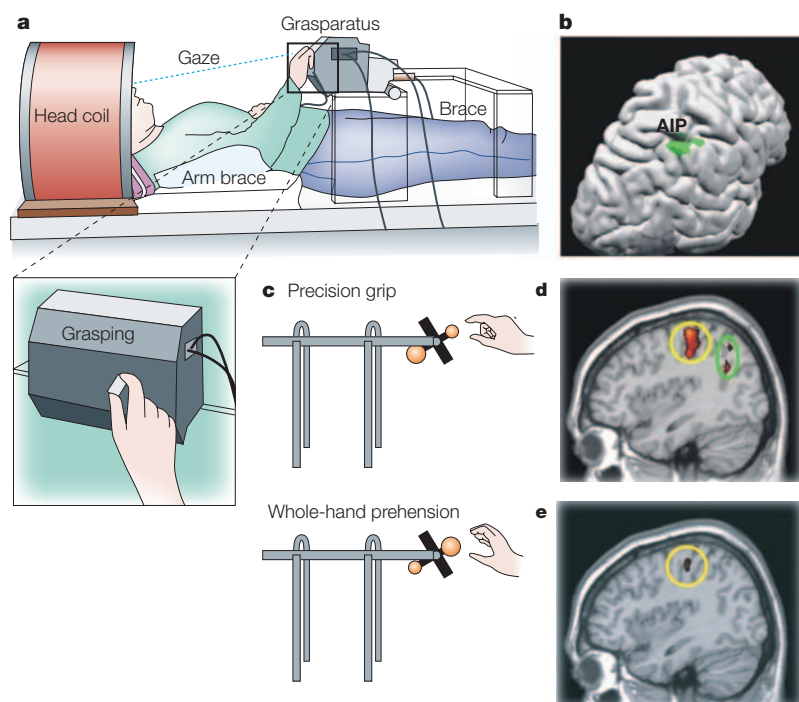


Figure 7 | Setups and results from two functional MRI grasping experiments. a | The 'grasparatus', a pneumatic rotating drum that was used to present objects that could be grasped with the right hand. **b** | This experiment showed the expected pattern of greater activation for grasping compared with reaching in the anterior intraparietal area (AIP; green). **c** | Grasping device used by Begliomini *et al.* (C. Begliomini, M. Wall, A. T. Smith and U.C., unpublished observations). Brain activations for precision grip (**d**) and whole-hand grasp (**e**). Yellow circles: activations detected in pre- and post-central gyrus (Brodmann area (BA) 3 and BA 4). Green circle: activations detected in the AIP (BA 40). Panel **b** modified, with permission, from REF. 95 © (2004) Oxford University Press.

two species difficult^{8–10}. Similarly, at a neural level, the evolutionary and functional differences among species are impossible to ignore^{101,102}.

Christel and colleagues⁴⁵ have suggested possible avenues to overcome these potential problems. They propose experiments in which humans perform reach-to-grasp actions in a crouched posture similar to macaques or in which monkeys are forced to sit with an upright posture similar to humans. However, this approach would impose movement constraints on the two species that might prevent the investigation of natural grasp kinematics. An alternative suggestion is to compare grasping behaviour in terms of the intended action to be performed rather than postural and behavioural differences. The comparison should be in terms of planning and control mechanisms¹⁰³ for grasping in a similar context.

Another issue is that testing in monkeys has been limited to variations in primitive geometric features of objects, such as size, shape and orientation^{60–65}. It seems important to extend studies to more 'cognitive' object characteristics, such as weight, fragility and surface texture. Although it can be difficult to train animals to perform these tasks, some situations that have already been investigated in humans could be studied in non-human primates. From a behavioural perspective, it is necessary to characterize whether monkeys adjust their

grip posture with respect to the shape of the object; whether they show different kinematics for different types of grasp; whether they show different kinematics with respect to the material from which the object they are aiming for is made; and whether contextual information is involved in the unfolding of the grasping action (for example, using the same object for different purposes). The last issue in particular is fundamental. 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 it⁷⁹. To compare species, it is necessary to discover whether and to what extent such variables also influence grasping in monkeys.

At the neurological level, the suggested homologies must also be viewed with caution. Some of the brain areas involved in the grasping circuit show evolutionary diversity. In particular, with respect to F1, monkeys have less ability than humans to move each finger in isolation^{104–106}, the parietal cortex differs greatly between humans and monkeys¹⁰¹ and the locus of a possible F5 in humans is still under debate¹⁰². Rizzolatti *et al.*⁹⁰ speculated that their findings "may indicate that in the monkey grasping movements are mediated by circuits different from those in humans". Importantly, in monkeys, the identification of components of the grasping circuit has been based on experiments in different monkeys, using different grasping tasks in different laboratories. We know little about the timing and extent of the neural discharge of different areas in the same monkey performing the same grasping task under the same conditions.

MULTI-ELECTRODE TECHNIQUES¹⁰⁷ might have the potential to identify the distinct roles of different areas in the planning and execution of grasping movements¹⁰⁸. In two unpublished studies, two macaques were trained to use different hand postures to reach and grasp six objects of various sizes and shapes (T. Brochier, M. A. Umiltá, R. L. Spinks and R. N. Lemon, unpublished observations; and M. A. Umiltá, T. Brochier, R. L. Spinks and R. N. Lemon, unpublished observations). Two multi-electrode drives were used to record simultaneously from small populations of single neurons in the primary motor cortex and F5 hand regions. The early results showed three populations of neurons with distinct functions in the planning and execution of grasp movements. In particular, these studies identified differences in the cortical activity for the six objects early in the task. They also showed how selective the activity for a given object was, and how it varied throughout the successive epochs of the task.

This type of neurophysiological study should be used to characterize the neural circuits that underlie the coding of intrinsic object properties and intentionality. It might be that the classic grasping circuit is overly simplistic, in as much as it does not include activity that might be recorded from areas that are concerned with object meaning (inferotemporal cortex) and/or with the decision of what to do with the object (for example, prefrontal lobes and cingulate cortex). Some hints that

MULTI-ELECTRODE TECHNIQUES

Allows the insertion of several glass-insulated platinum electrodes (diameter 80 μm) into the cortex in a 4-by-4 grid with an inter-electrode spacing of only 300 μm . Each electrode can be independently positioned.

DIFFUSION TENSOR IMAGING (DTI). This method can provide quantitative information with which to visualize and study connectivity and continuity of neural pathways in the central and peripheral nervous systems *in vivo*.

TRANSCRANIAL MAGNETIC STIMULATION (TMS). TMS involves creating a strong localized transient magnetic field that induces current flow in underlying neural tissue, causing a temporary disruption of activity in small regions of the brain.

the above factors are part of an overall grasping plan emerge from recently proposed neurophysiological models for grasping¹⁰⁹, neuroimaging studies on neurologically healthy subjects^{91–98} and studies of patients with neurological diseases^{76,94}.

Imaging studies indicate that a grasping circuit similar to that of the monkey can be broadly identified in humans, but also that a much wider network of areas is engaged. However, experiments in monkeys indicate that it might be necessary to conduct more extensive experiments to characterize brain activation across a wide range of grasping tasks, to show where in the human brain the different hand postures are stored. Furthermore, the predictions made regarding the neural substrates of human grasping have been based almost entirely on monkey data, and in some cases only a specific area (AIP) has been targeted^{93–96}. Although such an approach provides specific and controlled experimental hypotheses, it takes no account of the much greater range of hand-related functions in humans, and therefore ignores the likelihood that several different association areas are involved in the control of human grasping.

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 fMRI techniques (such as DIFFUSION TENSOR IMAGING; DTI)^{110–112} 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.

Another concern relates to the difficulty in pinpointing specific grasping areas in neuropsychological studies. Interpretation of neuropsychological findings is often difficult because lesions cover a large territory

and the function of areas that are not directly affected by the lesion might also be modified. However, a promising technique to overcome these potential problems is TRANSCRANIAL MAGNETIC STIMULATION (TMS)¹¹³. TMS allows temporary and circumscribed ‘virtual lesions’ to be induced in healthy humans. Recent work has shown that the ‘virtual’ lesions produced by TMS have the potential to reveal important facts about the neural networks that mediate grasping^{114,115}. For example, repetitive TMS applied to the left SPL as participants reached to grasp objects that could suddenly change in size indicates that this area might be crucial for the on-line control of grasping. The future might lie in combining TMS with activation data to study functional connectivity during grasping¹¹⁶.

The idea of combining different techniques might be the best way forward when it comes to comparing grasping in humans and non-human primates. Ideally, a coordinated series of neuroimaging experiment 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 it possible to carry out electrophysiological and possibly kinematic recording in both species during scanning¹¹⁷.

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 from the brain and behaviour, that we might completely understand the grasping function of the human hand.

- Bell, C. *The Hand: its Mechanisms and Vital Endowments as Evincing Design* (William Pickering, London, 1834).
 - Napier, J. R. *Hands* (George Allen & Unwin Ltd, London, 1980).
 - Napier, J. R. Studies of the hands of living primates. *Proc. Zool. Soc.* **134**, 647–657 (1960).
 - Napier, J. R. Prehensibility and opposability in the hands of primates. *Symp. Zool. Soc.* **5**, 115–132 (1961).
 - Bennett, K. M. B. & Castiello, U. *Insights into the Reach to Grasp Movement* (Elsevier Science, Amsterdam, 1994).
 - Wing, A. M., Haggard, P. & Flanagan, J. R. *Hand and Brain: the Neurophysiology and Psychology of Hand Movements* (Academic, San Diego, 1996).
 - Wilson, F. R. *The Hand* (Vintage Books, New York, 1998).
- References 5–7 are books that comprehensively cover the main aspects of grasping.**
- Susman, R. L. Hand of *Paranthropus robustus* from member 1, Swartkrans. *Science* **240**, 781–784 (1988).
 - Christel, M. in *Hands of Primates* (eds Preushoff, H. & Chivers, D. J.) 91–108 (Springer, New York, 1993).
 - Marzke, M. W. in *Insights into the Reach to Grasp Movement* (eds Bennett, K. M. B. & Castiello, U.) 19–35 (Elsevier Science, Amsterdam, 1994).
 - Jeannerod, M. in *Attention and Performance IX* (eds Long, J. & Baddeley, A.) 153–168 (Erlbaum, Hillsdale, 1981).
- This paper was the first to characterize kinematically the reach-to-grasp movement in humans. This seminal work laid the foundation of much of our current understanding of grasping.**
- Jeannerod, M. The timing of natural prehension movements. *J. Mot. Behav.* **16**, 235–254 (1984).
 - Jakobson, L. S. & Goodale, M. A. Factors affecting higher-order movement planning: a kinematic analysis of human prehension. *Exp. Brain Res.* **86**, 199–208 (1991).
 - Paulignan, Y., Jeannerod, M., Mackenzie, C. L. & Marteniuk, R. G. Selective perturbation of visual input during prehension movements. 2. The effects of changing object size. *Exp. Brain Res.* **87**, 407–420 (1991).
 - Gentiluoci, M. *et al.* Influence of different types of grasping on the transport component of prehension movements. *Neuropsychologia* **29**, 361–378 (1991).
 - Chieffi, S. & Gentiluoci, M. Coordination between the transport and the grasp component during prehension movements. *Exp. Brain Res.* **94**, 471–477 (1993).
 - Castiello, U., Bennett, K. M. B. & Stelmach, G. E. The bilateral reach to grasp movement. *Behav. Brain Res.* **1**, 43–57 (1993).
 - Weir, P. L. in *Insights into the Reach to Grasp Movement* (eds Bennett, K. M. B. & Castiello, U.) 129–150 (Elsevier Science, Amsterdam, 1994).
 - Castiello, U. Grasping a fruit: selection for action. *J. Exp. Psychol. Hum. Percept. Perform.* **22**, 582–603 (1996).
 - Paulignan, Y., Frak, V. G., Toni, I. & Jeannerod, M. Influence of object position and size on human prehension movements. *Exp. Brain Res.* **114**, 226–234 (1997).
 - Castiello, U. Mechanisms of selection for the control of hand action. *Trends Cogn. Sci.* **3**, 264–271 (1999).
 - Smeets, J. B. J. & Brenner, E. A new view on grasping. *Mot. Cont.* **3**, 237–271 (1999).
- An excellent review of experimental studies showing the influences of object properties on grasping behaviour.**
- Savelsbergh, G. J. P., Steenbergen, B. & van der Kamp, J. The role of fragility information in the guidance of the precision grip. *Hum. Mov. Sci.* **15**, 115–127 (1996).
 - Bootsma, R. J., Marteniuk, R. G., MacKenzie, C. L. & Zaaf, F. T. J. M. The speed-accuracy trade off in manual prehension: effects of movement amplitude, object size and object width on kinematic characteristics. *Exp. Brain Res.* **98**, 535–541 (1994).
 - Weir, P. L., MacKenzie, C. L., Marteniuk, R. G. & Cargoe, S. L. Is object texture a constraint on human prehension?: kinematic evidence. *J. Mot. Behav.* **23**, 205–210 (1991).
 - Weir, P. L., MacKenzie, C. L., Marteniuk, R. G., Cargoe, S. L. & Fraser, M. B. The effects of object weight on the kinematics of prehension. *J. Mot. Behav.* **23**, 192–204 (1991).
 - Johansson, R. S. & Westling, G. Coordinated isometric muscle commands adequately and erroneously programmed for the weight during lifting task with precision grip. *Exp. Brain Res.* **71**, 59–71 (1988).
 - Gordon, A. M., Forssberg, H., Johansson, R. S. & Westling, G. Visual size cues in the programming of manipulative forces during precision grip. *Exp. Brain Res.* **83**, 477–482 (1991).
 - Cuijpers, R. H., Smeets, J. B. J. & Brenner, E. On the relation between object shape and grasping kinematics. *J. Neurophysiol.* **91**, 2598–2606 (2004).
 - Santello, M. & Soechting, J. F. Gradual molding of the hand to object contours. *J. Neurophysiol.* **79**, 1307–1320 (1998).
 - Santello, M. & Soechting, J. F. Force synergies for multifingered grasping. *Exp. Brain Res.* **133**, 457–467 (1998).

32. Santello, M., Flanders, M. & Soechting, J. F. Patterns of hand motion during grasping and the influence of sensory guidance. *J. Neurosci.* **22**, 1426–1435 (2002).
33. Schieber, M. H. & Santello, M. Hand function: peripheral and central constraints on performance. *J. Appl. Physiol.* **96**, 2293–2300 (2004).
34. Mason, C. R., Gomez, J. E. & Ebner, T. J. Hand synergies during reach-to-grasp. *J. Neurophysiol.* **86**, 2896–2910 (2001).
35. Mason, C. R., Theverapperuma, L. S., Hendrix, C. M. & Ebner, T. J. Monkey hand postural synergies during reach-to-grasp in the absence of vision of the hand and object. *J. Neurophysiol.* **91**, 2826–2837 (2004).
36. Smeets, J. B. J., Brenner, E. & Biegstraaten, M. Independent control of the digits predicts an apparent hierarchy of visuomotor channels in grasping. *Behav. Brain Res.* **136**, 427–432 (2002).
37. Smeets, J. B. J. & Brenner, E. Independent movements of the digits in grasping. *Exp. Brain Res.* **139**, 92–100 (2001).
38. Castiello, U., Bennett, K. M. M. & Stelmach, G. E. Reach-to-grasp: the natural response to perturbation of object size. *Exp. Brain Res.* **94**, 163–178 (1993).
39. Edin, B. B. & Johansson, R. S. Skin strain patterns provide kinaesthetic information to the human central nervous system. *J. Physiol. (Lond.)* **487**, 243–251 (1995).
40. Johansson, R. S. in *Hand and Brain: the Neurophysiology and Psychology of Hand Movements* (eds Wing, A. M., Haggard, P. & Flanagan, J. R.) 381–414 (Academic, San Diego, 1996).
41. Johansson, R. S. in *Sensory Guidance of Movement. Novartis Found. Symp.* 219 (eds Block, G. R. & Goode, J. A.) 45–63 (John Wiley, New York, 1998).
42. Whitney, A. G., Wing, A., Thonnard, J. L. & Smith, A. M. The cutaneous contribution to adaptive precision grip. *Trends Neurosci.* **27**, 637–643 (2004).
43. Faugier-Grimaud, S., Frenois, C. & Stein, D. G. Effects of posterior parietal lesions on visually guided behaviour in monkeys. *Neuropsychologia* **16**, 151–168 (1978).
44. Roy, A. C., Paulignan, Y., Farné, A., Joffrais, C. & Boussaoud, D. Hand kinematics during reaching and grasping in the macaque monkey. *Behav. Brain Res.* **117**, 75–82 (2000).
45. Christel, M. I. & Billard, A. Comparison between macaques' and humans' kinematics of prehension: the role of morphological differences and control mechanisms. *Behav. Brain Res.* **131**, 169–184 (2002).
- References 44 and 45 show differences and similarities in the kinematics of grasping between humans and monkeys.**
46. Lawrence, D. G. & Hopkins, D. A. The development of motor control in the rhesus monkey: evidence concerning the role of corticomotoneuronal connections. *Brain* **99**, 235–254 (1976).
47. Lawrence, D. G. & Kuypers, H. G. The functional organization of the motor system in the monkey. I. The effects of bilateral pyramidal lesions. *Brain* **91**, 1–14 (1968).
48. Lawrence, D. G. & Kuypers, H. G. 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 (1968).
49. Muir, R. B. & Lemon, R. N. Corticospinal neurons with a special role in precision grip. *Brain Res.* **261**, 312–316 (1983).
50. Porter, R. & Lemon, R. N. in *Corticospinal Function and Voluntary Movement* (Oxford Univ. Press, Oxford, 1993).
51. Hepp-Reymond, M. C., Huesler, E. J. & Maier, M. A. in *Hand and Brain: the Neurophysiology and Psychology of Hand Movements* (eds Wing, A. M., Haggard, P. & Flanagan, J. R.) 37–62 (Academic, San Diego, 1996).
52. Gibson, A. R., Horn, K. M. & Van Kan, P. L. E. in *Insights into the Reach to Grasp Movement* (eds Bennett, K. M. B. & Castiello, U.) 129–150 (Elsevier Science, Amsterdam, 1994).
53. Smith, A. M. & Boubonnais, D. Neural activity in cerebellar cortex related to control of prehensile force. *J. Neurophysiol.* **45**, 286–303 (1981).
54. Robertson, E. M. Neural features of the reach and grasp. *Mot. Control* **4**, 117–120 (2000).
55. Jeannerod, M., Arbib, A., Rizzolatti, G. & Sakata, H. Grasping objects: the cortical mechanisms of visuomotor transformation. *Trends Neurosci.* **18**, 314–320 (1995).
- An excellent review of the neural mechanisms of grasping. It also provides insightful suggestions with regard to the application of computational modelling to grasping neurophysiology.**
56. Matelli, M., Luppino, G. & Rizzolatti, G. Patterns of cytochrome oxidase activity in the frontal agranular cortex of the macaque monkey. *Behav. Brain Res.* **18**, 125–136 (1985).
- An important paper that presents the cytoarchitectonics of the monkey's premotor cortex.**
57. Matelli, M. & Rizzolatti, G. Anatomic-functional organization of the agranular frontal cortex in primates. *Electroencephal. Clin. Neurophysiol. Electromyogr. Mot. Cont.* **97**, S8 (1995).
58. Luppino, G., Murata, A., Govoni, P. & Matelli, M. Largely segregated parietofrontal connections linking rostral intraparietal cortex (areas AIP and VIP) and the ventral premotor cortex (areas F5 and F4). *Exp. Brain Res.* **128**, 181–187 (1999).
59. Matelli, M. & Luppino, G. Parietofrontal circuits for action and space perception in the macaque monkey. *Neuroimage* **14**, 27–32 (2001).
60. Rizzolatti, G. *et al.* 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 (1988).
- This paper described the identification of the F5 neurons that are responsible for specific types of grasp.**
61. Taira, M., Mine, S., Georgopoulos, A. P., Murata, A. & Sakata, H. Parietal cortex neurons of the monkey related to the visual guidance of hand movement. *Exp. Brain Res.* **83**, 29–36 (1990).
62. Sakata, H., Taira, M., Murata, A. & Mine, S. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cereb. Cortex* **5**, 429–438 (1995).
63. Rizzolatti, G., Luppino, G. & Matelli, M. The organization of the cortical motor system: new concepts. *Electroencephalogr. Clin. Neurophysiol.* **106**, 283–296 (1998).
64. Murata, A., Gallese, V., Luppino, G., Kaseda, M. & Sakata, H. Selectivity for the shape, size, and orientation of objects for grasping in neurons of monkey parietal area AIP. *J. Neurophysiol.* **83**, 2580–2601 (2000).
65. Murata, A. *et al.* Object representation in the ventral premotor cortex (area F5) of the monkey. *J. Neurophysiol.* **78**, 2226–2230 (1997).
66. Rizzolatti, G., Fogassi, L. & Gallese, V. Parietal cortex: from sight to action. *Curr. Opin. Neurobiol.* **7**, 562–567 (1997).
67. Rizzolatti, G., Fogassi, L. & Gallese, V. Motor and cognitive functions of the ventral premotor cortex. *Curr. Opin. Neurobiol.* **12**, 149–154 (2002).
- An important review that summarizes the organization of the ventral premotor cortex and discusses in detail some of the higher functions of premotor areas.**
68. Fagg, A. H. & Arbib, M. A. Modeling parietal-premotor interactions in primate control of grasping. *Neural Networks* **11**, 1277–1303 (1998).
69. Fogassi, L. *et al.* Cortical mechanism for the visual guidance of hand grasping movements in the monkey: a reversible inactivation study. *Brain* **124**, 571–586 (2001).
- The inactivation of area F5ab produced a selective deficit of visually guided hand shaping producing hand postures that were not appropriate for the size and shape of the object. The specificity of the deficits caused by F5ab lesion indicates that this F5 sector has a crucial role in visuomotor transformation for object interaction.**
70. Gallese, V., Fadiga, L., Fogassi, L., Luppino, G. & Murata, A. in *Parietal Lobe Contributions to Orientation in 3D Space* (eds Thiers, P. & Karnath, H. O.) 255–270 (Springer, Berlin, 1997).
71. Gallese, V., Murata, A., Kaseda, M., Niki, N. & Sakata, H. Deficit of hand reshaping after muscimol injection in monkey parietal cortex. *Neuroreport* **5**, 1525–1529 (1994).
72. Gardner, E. P., Debow, D. J., Ro, J. Y., Ghosh, S. & Srinivasa, B. Sensory monitoring of prehension in the parietal lobe: a study using digital video. *Behav. Brain Res.* **135**, 213–224 (2002).
73. Denny-Brown, D. Disintegration of motor function resulting from cerebral lesions. *J. Nerv. Ment. Dis.* **112**, 1–45 (1950).
74. Lassek, A. M. in *The Pyramidal Tract: Its Status in Medicine* (Charles C. Thomas, Springfield, 1954).
75. Lang, C. E. & Schieber, M. H. Reduced muscle selectivity during individuated finger movements in humans after damage to the motor cortex or corticospinal tract. *J. Neurophysiol.* **91**, 1722–1733 (2004).
76. Binkofski, F. *et al.* Human anterior intraparietal area subserves prehension. *Neurology* **50**, 1253–1259 (1998).
- An excellent and comprehensive neuropsychological and fMRI study showing that the AIP can be considered to be the area of grasping in humans, as it is in monkeys.**
77. Glover, S. Optic ataxia as a deficit specific to the on-line control of actions. *Neurosci. Biobehav. Rev.* **27**, 447–456 (2003).
- An important review that proposes a new theoretical approach to optic ataxia.**
78. Rossetti, Y., Vighetto, A. & Pisella, L. Optic ataxia revisited: immediate motor control versus visually guided action. *Exp. Brain Res.* **153**, 171–179 (2003).
79. Jeannerod, M. Mechanisms of visuomotor coordination: a study in normal and brain-damaged subjects. *Neuropsychologia* **24**, 41–78 (1986).
- The first paper to describe the kinematics of grasping abnormalities in patients with optic ataxia.**
80. Jakobson, L. S., Archibald, Y., Carey, D. & Goodale, M. A. A kinematic analysis of reaching and grasping movements in a patient recovering from optic ataxia. *Neuropsychologia* **29**, 803–809 (1991).
81. Milner, A. D., Dijkerman, H. C., McIntosh, R. D., Rossetti, Y. & Pisella, L. Delayed reaching and grasping in patients with optic ataxia. *Prog. Brain Res.* **142**, 225–242 (2003).
82. Milner, A. D. *et al.* Grasping the past: delay can improve visuomotor performance. *Curr. Biol.* **11**, 1896–1901 (2001).
83. Jeannerod, M., Decety, J. & Michel, F. Impairment of grasping movements following a bilateral posterior parietal lesion. *Neuropsychologia* **32**, 369–380 (1994).
- An important study showing that grasping abnormalities in a patient with a posterior parietal lesion occurred for neutral geometric objects but not for familiar visual objects.**
84. Galletti, C., Fattori, P., Kutz, D. F. & Battaglini, P. P. Arm movement-related neurons in the visual area V6A of the macaque superior parietal lobule of special interest. *Eur. J. Neurosci.* **9**, 410–413 (1997).
85. Milner, A. D. in *Parietal Lobe Contributions to Orientation in 3D Space* (eds Thiers, P. & Karnath, H. O.) 3–22 (Springer, Berlin, 1997).
86. Decety, J. in *Insights into the Reach to Grasp Movement* (eds Bennett, K. M. B. & Castiello, U.) 109–126 (Elsevier Science, Amsterdam, 1994).
87. Grafton, S. T., Fagg, A. H., Woods, R. P. & Arbib, M. A. Functional anatomy of pointing and grasping in humans. *Cereb. Cortex* **6**, 226–237 (1996).
88. Matsumura, M. *et al.* Changes in rCBF during grasping in humans examined by PET. *Neuroreport* **7**, 749–752 (1996).
89. Faillet, I., Toni, I., Decety, J., Gregoire, M. C. & Jeannerod, M. Visual pathways for object-oriented action and object recognition: functional anatomy with PET. *Cereb. Cortex* **7**, 77–85 (1997).
90. Rizzolatti, F. *et al.* Localization of grasp representations in humans by PET: 1. Observation versus execution. *Exp. Brain Res.* **111**, 246–252 (1996).
91. Castiello, U. *et al.* Human inferior parietal cortex 'programs' the action class of grasping. *Cogn. Syst. Res.* **1**, 89–97 (1998).
92. Grafton, S. T., Fagg, A. H. & Arbib, M. A. Dorsal premotor cortex and conditional movement selection: a PET functional mapping study. *J. Neurophysiol.* **79**, 1092–1097 (1998).
93. Culham, J. C. *et al.* Visually-guided grasping produces activation in dorsal but not ventral stream brain areas. *Exp. Brain Res.* **153**, 158–170 (2003).
- An expertly conducted study that convincingly shows increased AIP activity during grasping tasks.**
94. James, T. W., Culham, J., Humphrey, G. K., Milner, A. D. & Goodale, M. A. Ventral occipital lesions impair object recognition but not object-directed grasping: an fMRI study. *Brain* **126**, 2463–2475 (2003).
95. Culham, J. in *Functional Neuroimaging of Visual Cognition: Attention and Performance XX* (eds Kanwisher, N. & Duncan, J.) 417–438 (Oxford Univ. Press, Oxford, 2004).
96. Frey, S. H., Vinton, D., Norlund, R. & Grafton, S. T. Cortical topography of human anterior intraparietal cortex active during visually guided grasping. *Cogn. Brain Res.* **23**, 397–405 (2005).
97. Grezes, J., Armony, L., Rowe, J. & Passingham, R. E. Activations related to 'mirror' and 'canonical' neurons in the human brain: an fMRI study. *Neuroimage* **18**, 928–937 (2003).
98. Chapman, H. *et al.* Posterior parietal cortex control of reach-to-grasp movements in humans. *Eur. J. Neurosci.* **15**, 2037–2042 (2002).
99. Ehrsson, H. H. *et al.* Cortical activity in precision- versus power-grip tasks: an fMRI study. *J. Neurophysiol.* **83**, 528–536 (2000).
100. Ehrsson, H. H., Fagergren, E. & Forssberg, H. Differential fronto-parietal activation depending on force used in a precision grip task: an fMRI study. *J. Neurophysiol.* **85**, 2613–2623 (2001).
101. Culham, J. C. & Kanwisher, N. G. Neuroimaging of cognitive functions in human parietal cortex. *Curr. Opin. Neurobiol.* **11**, 157–163 (2001).
- An insightful review of the cognitive functions in human parietal cortex. It also provides a comparison of human and monkey parietal cortex.**

102. Amunts, K. *et al.* Broca's region revisited: cytoarchitecture and intersubject variability. *J. Comp. Neurol.* **412**, 319–341 (1999).
103. Glover, S. Separate visual representations in the planning and control of action. *Behav. Brain Sci.* **27**, 3–78 (2004).
104. Kimura, D. & Vanderwolf, C. H. The relation between hand preference and the performance of individual finger movements by left and right hand. *Brain* **93**, 769–774 (1970).
105. Schieber, M. H. Individuated finger movements of rhesus monkeys: a means of quantifying the independence of the digits. *J. Neurophysiol.* **65**, 1381–1391 (1991).
106. Sanes, J. N. & Schieber, M. H. Orderly somatotopy in primary motor cortex: does it exist? *Neuroimage* **13**, 968–974 (2001).
107. Eckhorn, R. & Thomas, U. A new method for the insertion of multiple microprobes into neural and muscular tissue, including fiber electrodes, fine wires, needles and microsensors. *J. Neurosci. Methods* **49**, 175–179 (1993).
108. Brochier, T., Spinks, R. L., Umiltà, M. A. & Lemon, R. N. Patterns of muscle activity underlying object-specific grasp by the macaque monkey. *J. Neurophysiol.* **92**, 1770–1782 (2004).
109. Rizzolatti, G. & Luppino, G. The cortical motor system. *Neuron* **31**, 889–901 (2001).
110. Basser, P. J. & Pajevic, S. *In vitro* fiber tractography using DT-MRI data. *Magn. Reson. Med.* **44**, 625–632 (2000).
111. Mori, S. & Kaufmann, W. K. *In vivo* visualization of human neural pathways by MRI. *Ann. Neurol.* **47**, 412–414 (2000).
112. Ramnani, N., Behrens, T. E. J., Penny, W. & Matthews, P. M. New approaches for exploring anatomical and functional connectivity in the human brain. *Biol. Psychiatry* **56**, 613–619 (2004).
113. Walsh, V. & Rushworth, M. F. S. A primer of magnetic stimulation as a tool for neuropsychology. *Neuropsychologia* **37**, 125–136 (1999).
114. Glover, S., Miall, R. C. & Rushworth, M. F. S. Parietal rTMS selectively disrupts the initiation of on-line adjustments to a perturbation of object size. *J. Cogn. Neurosci.* **17**, 124–136 (2005).
115. Cattaneo, L. *et al.* A cortico-cortical mechanism mediating object-driven grasp in humans. *Proc. Natl Acad. Sci. USA* **102**, 898–903 (2005).
116. Paus, T. *et al.* Transcranial magnetic stimulation during positron emission tomography: a new method for studying connectivity of the human cerebral cortex. *J. Neurosci.* **17**, 3178–3184 (1997).
117. Logothetis, N. K., Guggenberger, H., Peled, S. & Pauls, J. Functional imaging of the monkey brain. *Nature Neurosci.* **2**, 555–562 (1999).

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Competing interests statement

The author declares no competing financial interests.