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The neural mechanisms of manual dexterity

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Abstract

The hand endows us with unparalleled precision and versatility in our interactions with objects, from mundane activities such as grasping to extraordinary ones such as virtuoso pianism. The complex anatomy of the human hand combined with expansive and specialized neuronal control circuits allows a wide range of precise manual behaviours. To support these behaviours, an exquisite sensory apparatus, spanning the modalities of touch and proprioception, conveys detailed and timely information about our interactions with objects and about the objects themselves. The study of manual dexterity provides a unique lens into the sensorimotor mechanisms that endow the nervous system with the ability to flexibly generate complex behaviour.

The hand is the most versatile manipulative organ in the known universe. Manual behaviour is epitomized by virtuoso pianism or assembling a clockwork mechanism, but everyday activities — such as grasping an object of arbitrary shape or opening a bottle — are challenging for even the most sophisticated robots[1]. For a long time, the study of the neural basis of manual behaviour was hindered by the challenges of characterizing the shape of the hand and the forces it exerts on objects. Recent advances in pose estimation and sensor technology (for examples, see REFs[2,3]), however, have set the stage for achieving new insights into manual dexterity and its neural underpinnings.

In this Review, we first discuss aspects of mundane manual behaviours, such as grasping, and of expert ones, such as playing a musical instrument. We then describe anatomical features of the hand that are key to its versatility and strength. Next, we explore what is known about the neural mechanisms that give rise to manual dexterity, both motor and sensory, highlighting those that appear to be specific to the hand. Finally, we identify

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outstanding questions about the neural basis of manual behaviour, focusing on systems where hand-related specializations are liable to be found.

Manual dexterity

Dexterity is defined as skilled behaviour involving the hands, although the manual connotation is often lost. In this Review, we define dexterity as precise, diverse and flexible behaviour that involves the coordination of many segments and whose repertoire can be expanded through learning. Quantifying the dexterity of the hand is challenging given its myriad functions, but analysis of even simple, well-studied manual behaviours such as grasping reveals great sophistication. When we reach to grasp an object, we preshape the hand to its shape. The precision and specificity of this preshaping is such that one can predict which of many objects is to be grasped from the hand's conformation, long before contact with the object is established[4–7]. Examination of this everyday manual behaviour reveals structure in hand postures. For example, the aperture of the hand is adjusted depending on the size of the object[6], which involves the coordinated flexion and extension of joints distributed over the five digits. Similarly, the spread (abduction) of the fingers is adjusted semi-independently depending on the shape and size of the object. While the movements of the fingers tend to be coordinated, movements of the thumb tend to be more independent[8,9].

Principal component analysis — which expresses hand kinematics in terms of correlated joint movements — reveals that manual behaviour during grasping can be well represented by a small number of principal components, called 'synergies'[5,6,10–15], which can be in part attributed to biomechanical constraints imposed by the musculoskeletal system[16]. This structure of prehensile hand movements has been interpreted as implying that the hand can only volitionally adopt a limited range of postures, confined to combinations of synergies. While this strategy simplifies the problem of controlling a hand, it also reduces the degrees of freedom of the hand — the number of (metaphorical) knobs required to control the hand.

An implication of the synergies hypothesis is that low- variance principal components simply reflect noise in the hand measurements or in the hand postures themselves. It turns out, however, that synergies fail to account for the exquisite precision of the hand. Indeed, the synergies hypothesis predicts that our ability to classify objects from precontact hand postures will break down after removal of the synergies (the first six to eight principal components), but this is not the case[7,17]. Rather, the object to be grasped can be predicted well above chance even after the first 20 synergies have been removed. In other words, the components of hand posture reflected in the low-variance principal components are under volitional control. If one were to control a hand with knobs, it would take more than 20 knobs to do so with the equivalent precision, and this is for grasping, a simple unskilled behaviour.

Skilled manual behaviour has not been studied as systematically as has grasping, hindered in part by contact with objects — prevalent during most manual behaviours and critical to understanding these — being difficult to measure. Nonetheless, simple metrics of skilled manual behaviour reveal the staggering rapidity and precision of the hand. Pianists can play more than 800 notes per minute with each hand[18], skilled typists can type 600 characters per minute[19] and professional gamers can execute 800 actions per minute[20]. Artists can draw submillimetre illustrations on a grain of rice or compose images of handwritten micrographic text[21]. Experienced Braille users can read more than 200 words per minute in Braille script, approaching the median visual rate of 250 words per minute[22]. Finger-tutters can fluidly execute remarkably complex hand postures[23]. These manual abilities are, however, acquired. Even moving individual fingers while keeping others still is difficult and does not come naturally[8,24–28,] and the finger individuation required for piano playing requires extensive training[29–31].

The inclination to use one or the other hand is strongly asymmetric in most individuals, and the preferred hand is the right one in 90% of adult humans[32], as is implied in the etymology of the word ‘dexterity’: *dextra* is the Latin word for ‘right hand’. By contrast, the distribution of handedness in other primates is symmetric[33–35], suggesting that the prevalence of right-handedness in humans might be culturally inherited[36], although innate differences are difficult to distinguish from acquired ones[37]. In adults, the differences in finger individuation between the dominant hand and the non-dominant hand are slight[38,39] as are the differences in the performance of simple tasks[40–42]. However, the performance gap between the dominant hand and the non-dominant hand for complex tasks such as writing is much wider and cannot be totally overcome, even with extensive training[43–45.]

Anatomical complexity of the human hand

The neural basis of dexterity cannot be understood without considering the musculoskeletal structure of the hand. All manual control is enabled by hand bio-mechanics, which define what can and cannot be done. More broadly, the neural mechanisms of control have evolved in tandem with the musculoskeletal features of the hand to give rise to dexterity.

Bones

The skeleton of the hand comprises 27 bones: five metacarpals of the palm, including a divergent thumb metacarpal, two phalanges of the thumb, three phalanges in each other digit and eight carpal bones that connect the hand to the forearm[46]. The bones of the hand and wrist are connected by a complex network of passive ligaments that stabilize all the elements and constrain their relative movements. Each bone moves in relation to neighbouring bones, forming numerous anatomical joints that allow at least 24 actively articulated degrees of freedom, including three at the wrist (with forearm-based rotation), four at each finger (with flexion–extension and abduction–adduction at metacarpophalangeal joints) and five at the thumb — three of which are at the base (flexion, abduction and rotation). Several other joints, including carpometacarpal joints, are also semi-independent and may contribute additional degrees of freedom. Development of the hand takes a long time[47]. Although the hand bones appear prenatally, ossification of the carpal bones starts several months after birth, with some emerging at 10 years of age, and the hand and wrist are fully developed only at 16–18 years of age.

The main feature of the human hand is the opposability of the thumb, which allows precise and versatile prehension. Although definitions of opposability differ, the main characteristic is the ability for the thumb to oppose and touch each of the other fingers at the tip[48,49]. Many but not all primates are endowed with some degree of opposability, ranging from pseudo-opposable thumbs — common in New World monkeys and prosimians — to semi-opposable thumbs — present in Old World monkeys and apes — to fully opposable thumbs — present only in humans. While pseudo-opposable thumbs can flex–extend and abduct–adduct, semi-opposable thumbs also rotate axially during abduction, thereby bringing the pad of the thumb towards the pads of other fingers. The rotation is made possible by the specialized saddle shape of the trapezium, the carpal bone that supports the thumb metacarpal. Full opposability, defined by broad contact between the pads of the thumb and the other fingers, is made possible by a relatively long thumb[50,51]. Toes in most monkeys and apes are also opposable, and can be used for grasping, while human feet support bipedalism and comprise toes that are not opposable[52]. Non-primates also possess prehensile ability and even opposing fingers, but none of their digits exhibits the complexity of movement of the primate thumb.

Muscles and tendons

The hand is articulated by 20 muscles located in the forearm and 21 muscles located in the hand itself (FIG. 1; Supplementary Tables S1–S3)[53]. Some muscles — especially muscles that drive the digits — comprise several semi-independently controlled heads on the distal side[26,54–56], increasing the number of controlled actuaors to 30 in the forearm and 22 in the hand, for a total of 52. Of these, 13 actuators articulate mainly the wrist, 11 the thumb and 28 the fingers.

Attachment of muscles to finger segments is different for flexors and extensors. Finger flexors attach their tendons directly to finger phalanges, with the deep flexor tendon threading through the superficial tendon to attach on the distal phalanx, allowing differentiated control of the distal joints and high strength. In addition to flexion, flexor muscles also adduct the fingers, bringing them together for a tight grasp. By contrast, extensors feed into the joined extensor sheath, which covers the dorsal aspect of each digit[57]. Pulling on one side of the sheath or the other deviates the finger into abduction or adduction[58,59]. Pulling both sides allows simultaneous flexion of the metacarpophalangeal joint and extension of interphalangeal joints. Moreover, the distal tendons of the extensors are interconnected, which limits finger individuation during extension[60].

The small internal hand muscles (lumbricals and interossei) are located mostly between metacarpals and distally attach to phalanges and to the extensor sheath. Lumbricals originate not from bones but from the tendons of the large deep finger flexors of the forearm. Although these muscles can transfer the tension caused by flexion to the extensor hood, their weakness and dense sensory innervation suggest that their primary role may be to act as high-precision sensors of hand posture[61]. The stronger palmar interosseus muscles also induce rotation of the fingers, which is critical for grasping.

The complexity of the musculature and of its attachments to the bones leads to a complex relationship between joint movement and muscle activation[62–67]. Many, if not all, hand muscles act across multiple joints, so torques produced around each joint must be counter-balanced to achieve desired joint postures. For example, finger flexion needs to be balanced by wrist extension torque. Antagonistic muscles are commonly activated together during hand movements to stiffen a joint against unwanted perturbations[62,68–73]. Furthermore, the torque-generating properties of muscles crossing a joint depend on the posture of that joint and that of all other joints the muscle crosses, further complicating the control problem[74–80]. Even simple hand postures or end point forces thus require the coordination of many muscles with articulations distributed over the entire hand.

In humans, a power grip entails a total maximum force of around 550 N, concentrated at the proximal metacarpophalangeal joints[81,82]. Digits 1, 2 and 3 can produce more force on average (120–137 N) than can digits 4 and 5 (57–96 N). Extrinsic finger flexors and extensors generally produce much higher forces (up to 20-fold) than intrinsic hand muscles[74,83], although this difference is more pronounced for some hand postures than others.

Hand variations

Sex differences in human hand anatomy and manual abilities are restricted mostly to variation in size[84–87]. Index fingers in males are more commonly shorter than ring fingers[88,89], and carpal bones differ subtly in shape and relative size, which may slightly affect the range of motion and dynamics of the digits[90–94]. Beyond sex, variability of the hand musculature between humans is not restricted to the volume, but commonly includes full separation of muscle compartments, additional heads, shifts in attachment points, disappearance of common muscles and reappearance of atavistic muscles[95–100].

Although the human hand is often described as unique in the animal kingdom for its complexity and versatility (BOX 1), many of its special muscular features are also found in the hands of apes and monkeys[53,101,102] (but see REF.[103]). For example, two thumb muscles that were thought to be unique to humans were later identified in gibbons and bonobos[104,105]. Similarly, humans share the anatomy of muscles that allow independent extension of index and little fingers with gorillas and chimpanzees[106]. Humans have fewer intrinsic hand muscles and, in some ways, possess a simplified primate hand. The increased complexity of non-human primate hands stems from the use of hands in locomotion — in trees or on the ground[48] — a function that human hands lack. The feats of human hands — such as playing the piano or assembling a clockwork mechanism — are enabled by superior neural control but also benefit from the narrower scope of manual behaviour in humans.

Cortical control of the hand

Cortical magnification

Given the sophistication of the hand and of manual behaviours, it should come as no surprise that large swaths of the nervous system are devoted to controlling it[107–113]. The primary motor cortex (M1) — the region of the neocortex that sends signals to the muscles via the spinal cord to drive movement — is coarsely organized in a somatotopic fashion, in which different parts of the brain contribute to movement of different parts of the body. The hand occupies an outsized proportion of the motor homunculus — the map of the body in M1. While the hand accounts for 0.6% of the body by weight and 2% by surface area, more than 20% of M1 is devoted to it as gauged by the tendency to evoke finger movements via electrical stimulation[112,114–117], and this phenomenon is even more pronounced on the side contralateral to the dominant hand[118–120]. In primates, and in particular higher primates, electrical stimulation of large swaths of the cortex outside M1 also evokes hand movement, implying widespread neuronal circuitry to support manual control[111,121].

Hand control signals in the cortex

M1 plays a critical role in dexterous manual behaviour as evidenced by the fact that lesions of M1 produce severe motor deficits, as do lesions of the descending pyramidal tract, the principal relay of motor signals from the cortex to muscles[122–128] (reviewed in REF.[129]). Over time, monkeys and humans recover the ability to grasp objects, but dexterous control and individuated finger movements never return, as precise spatio-temporal patterns of muscle activation remain disturbed[130] and overly synchronized[131]. In humans, extensive rehabilitation in patients with pure motor hemiparesis can lead to partial recovery of thumb and index finger independence, but the selectivity of muscle recruitment never fully recovers[132,133].

The principles that underlie the coding structure in the M1 hand representation are unclear. Individual neurons in M1 drive movement across multiple joints distributed over the entire hand, often including digits and the wrist[110,134,135]. The tendency of individual neurons to drive combinations of joints cannot be explained solely by the proximity of the joints, their tendency to move together or their muscular articulation[110,135,136]. These response properties reflect both the aforementioned complexity of the muscular articulation of the hand and the fact that individual pyramidal neurons in M1 project to multiple spinal motor neuron nuclei[137]. As might be expected given the prevalence of multi-joint response fields, the somatotopic organization in the M1 hand representation — and across the motor homunculus — is coarse. The hand representation in M1 overlaps with that of the proximal limb, and representations of digits and the wrist are inextricably intertwined[138,139].

Proximal limb-related neurons in M1 produce a strong phasic response during movement and a much weaker tonic response during maintained posture. By contrast, hand-related neurons encode the time-varying posture and do not exhibit a preference for movement[135]. Another difference lies in the dynamics of the responses at the population level. When monkeys perform reaching movements, population responses in M1 exhibit smooth dynamics; that is, the present neural state predicts the future neural state[140]. This population-level behaviour is consistent with a role for M1 as a pattern generator that ultimately drives muscles to give rise to movement. However, M1 does not exhibit smooth dynamics during grasping movements when the reach component is eliminated, for example when catching or grasping an object that is handed to you[141]. Population dynamics during reach to grasp seem to be intermediate between those of reach and those of grasp[142,143]. The population-level response, then, is very different for manual behaviour than it is for its proximal limb counterpart. One possible explanation for this observation is that these differences in neuronal activity — at the single-cell and population levels — reflect fundamentally different control strategies for arms versus hands. Another possibility is that they reflect differences in the biomechanics of the effectors: arms are much heavier than fingers, so arm movements may require characteristically different muscle activations, which in turn involve different neuronal dynamics in M1.

M1 participates not only in controlling hand movements but also in controlling the manual application of forces. During reach, corticospinal input is strongest for forearm muscles, but as fingers close around the object, the focus shifts to intrinsic hand muscles[144]. Neurons in M1 exhibit a transient burst of activity that encodes grasp force[145–151] followed by a tonic response that is much weaker but nonetheless carries grasp force information[152].

M1 also has a role in modulating spinal reflexes and gating sensory inputs[153–157]. Indeed, while spinal reflexes are often thought to contribute to only stereotyped and unattended behaviours, such as locomotion, the modulation of these reflexes also plays a role in prehensile behaviours[158–163]. For example, reflexes can stabilize the hand and wrist and facilitate object interactions during grasp, so the suppression of these reflexes is relieved in anticipation of a grasp[163–166]. Although M1 and auxiliary structures, including the supplementary motor area, are implicated in this modulation, dense efferent projections from the ventral cingulate motor area onto spinal interneurons might also play an important role[113,167–170]. The modulation of reflexes is an integral part of motor control, and hand control is no exception.

Bypassing spinal circuitry

The hand representation in M1 not only is large but also has privileged access to the muscles. While most signals from M1 are sent to the muscles via spinal interneurons, a subpopulation of pyramidal neurons — the so-called corticomotoneuronal (CM) cells (FIG. 2), located mostly in the caudal aspect of M1 — synapse directly onto spinal motor neurons, thereby bypassing spinal interneurons[171–176]. Individual CM cells drive multiple downstream muscles[139,177–179], are active throughout movement and posture phases[148,180,181], recruit muscles selectively for specific functions[181,182] and are involved in transcortical reflex loops[183–185] (for a review, see REF.[186]). Although still only sparsely characterized, the behaviour of CM cells is consistent with the hypothesis that they each enable activation of a combination of muscles that contributes to a specific movement (see, however, REF.[187] for an alternative hypothesis). According to this view, populations of CM cells allow a more direct access to a wider repertoire of movements than can be achieved solely through polysynaptic projections to the muscles. Such a broad repertoire of control signals could, in principle, allow the generation of movements that bypass the polysynaptic pathways or the refinement of movements generated through polysynaptic pathways[154].

While CM cells synapse onto motor neurons innervating most if not all muscles and are active during both complex and simple movements[188–192], two lines of circumstantial evidence suggest that these neurons are critical for dexterous manual behaviours such as precision grasp and individuated finger movements[173,174,193–199]. First, lesions that target the CM pathway impair dexterity, resulting in reductions in the speed of hand movements, the magnitude of manually applied forces and the degree of finger individuation, as well as permanent deficits in the ability to preshape the hand during grasp[153,200]. These deficits are exacerbated when lesions extend to other corticospinal projections[201]. Second, primates with CM cells tend to exhibit greater dexterity than those without them. While fair comparison of dexterity between species is challenging because of differences in the musculoskeletal structure of the hand[50,196,202,203], comparison of species with similar hand anatomy implicates the CM pathway. For example, capuchins and squirrel monkeys both have pseudo-opposable thumbs and very similar hand structures, but the projections from M1 to the ventral spinal cord are dense in capuchins and sparse in squirrel monkeys[204,205] (FIG. 2). Correspondingly, capuchins use individual fingers for grasping, while squirrel monkeys do not. The search for an involvement of the CM pathway in dexterity outside the primate order has also come up empty. Notably, some carnivores anecdotally known for their manipulative ability — raccoons[206–208] and kinkajous[209] — have been suspected of having CM connections, but the electrophysiological evidence does not support the existence of a monosynaptic pathway[210] and, upon closer examination, their grasps are not as varied as are those of primates[211].

In one study, causal evidence was provided for the role of CM cells in dexterity by exploitation of the fact that early postnatal mice have CM cells that are eliminated later in life[212]. Preservation of CM cells through genetic manipulation led to increased dexterity, as indexed by a higher success rate in grasping and manipulation tasks, although still much lower than in primates. One interpretation of this finding is that the cortex sculpts the input–output relationship of the spinal cord circuits in newborn mice via CM connections to produce a desired set of behaviours. After the behaviour has been established and consolidated via spinal interneurons, the now redundant CM pathway is eliminated, presumably because it requires energy to be maintained and adds unnecessary complexity to the neural circuits of motor control. In this view, humans and many primates retain the ability to learn complex new movement patterns in adulthood in part because CM connections are preserved.

While the relationship between CM cells and manual dexterity is debated, no organism capable of highly individuated finger movements has been reported to lack CM connections.

Visual guidance of hand movements

Successful interactions with the environment typically entail forming appropriate motor plans to interact with objects on the basis of visual information about the objects' location and shape. The primate brain comprises specialized circuits — located in the posterior parietal cortex (PPC) — to achieve this visuomotor transformation[213–220] (FIG. 3). Indeed, damage to the PPC in humans leads to varied deficits in manual behaviour, including constructional apraxia — the inability to copy an image or mimic a movement with the affected hand[221]. The PPC contains many regions that can be separated on the basis of architectonic, connective and functional differences[221–223], two of which have been implicated in dexterity, namely the parietal reach region (PRR) and the anterior intraparietal area (AIP).

The PRR has a role in planning reaches to visually guided locations in peripersonal space[213,216,224–229]. Neuronal activity in the PRR correlates with movement direction during planning, and its disruption shortly before movement onset leads to reaches that start out in the wrong direction[230,231]. Neurons in the PRR encode limb movement in eye-centred coordinates, as evidenced by a systematic dependence of neuronal responses on gaze direction. The PRR not only is involved in planning specific reaches but also may simultaneously encode multiple reaches and contribute to the decision about which movement to execute[232–236]. Beyond mediating visuomotor transformations, the PRR is implicated in converting other sensory reference frames (for example, auditory) to eye-centred ones[226,237,238].

The AIP has a crucial role in visually guided hand control; for example, in preshaping the hand to grasp an object[220,239–247]. Neurons in the AIP exhibit visual responses that are dependent on the shape of the object and its position in eye-centred coordinates[241,248–250]. At the population level, AIP neurons encode not only object shape but also planned grip type[220]. Reversible inactivation of the AIP leads to an inability to preshape the hand to the object but it does not interfere with the reach[251–253] (for a review, see REF.[254]). The AIP projects to the ventral premotor area, where neurons also exhibit selective tuning to the object shape and grasp but encode more motor-related information[255–258].

The PPC thus has a role in planning reaching and grasping movements, whereas M1 is involved with the execution of these movements[259,260]. Both the PRR and the AIP are involved in converting a visual representation of an object — initially in an eye-centred coordinate frame — into a motor representation of the object to give rise to appropriate arm and hand movements to grasp or manipulate it. Both cortical fields project to the premotor cortex, where the motor plan is further refined before it is conveyed to M1 (REFs[170,261–268]). The role of the PPC in prehension is further supported by the observation of a direct connection to spinal hand premotor interneurons in primates[269] and by reports that intracortical microstimulation of the PPC evokes hand movements[111,270,271] (but see REF.[272]). Although they are important for primates, visuomotor transformations are less important for mice and rats, and these rodent species have no well-established homologues to the PPC of primates[273].

Sensory mechanisms of dexterity

Manual dexterity depends not only on an elaborate end effector and sophisticated neural mechanisms of control but also on two exquisite sensory systems. Proprioception tracks the movements of the hand and the muscular effort exerted by hand muscles. Touch conveys information about the objects with which we interact and about our interactions with them. Individuals who have lost their senses of touch and proprioception — as a result of peripheral neuropathies, genetic mutations, vitamin and mineral deficiencies, immune diseases, cancer or posterior spinal cord lesions — develop severe movement disorders, which are particularly pronounced for hand use[274–285]. Indeed, visual guidance of behaviour — and in particular manual behaviour — is a poor substitute for its somatosensory counterparts. The somatosensory and motor systems are tightly coupled, and manual dexterity is predicated upon their interplay[286,287].

Tactile and proprioceptive sensitivity

Our sense of touch is exquisitely sensitive, particularly to dynamic stimuli. We can detect skin vibrations on the order of a tenth of a micrometre (at 250 Hz, where sensitivity peaks)[288], a 50th of the average diameter of a human hair. When we run our hand across a surface, we can discern a textural element on a scale of tens of nanometres[289]. However, when the skin is indented by an object or surface, without tangential movement, tactile sensitivity to spatial features drops dramatically. Two pinpoint touches need to be 1 mm apart to be discerned as separate[290], a groove needs to be 1-mm wide before we are able to make out its orientation[291] and textures with elements in the submillimetre range feel smooth[292]. Even our ability to detect a touch is severely compromised if the indentation happens very slowly[293]. Angular acuity — the change in the orientation that can be detected — is around 10–20° for edges indented into or scanned across the skin, almost four times that for visually presented edges after differences in innervation density have been accounted for[294,295]. However, the tactile angular acuity is equivalent to its visual counterpart — on the order of 5° — when tested in the context of object manipulation[296].

Neural basis of somatosensation

The exceptional sensitivity of the palmar surface of the hand is conferred by the approximately 17,000 nerve fibres that carry tactile signals to the CNS[297]. Each fibre innervates one of four types of mechanoreceptors that tile the glabrous skin (hairless skin) of the hand, each of which responds to different aspects of a skin deformation[298–300]. Two types of nerve fibres — rapidly adapting and Pacinian corpuscle-associated fibres, which innervate Meissner and Pacinian corpuscles, respectively — are sensitive to skin vibrations and respond robustly when the fingers move across a textured surface. A third type of nerve fibre, slowly adapting type 1 fibre, which innervates Merkel receptors, produces a graded response to pressure exerted on the skin and is especially sensitive to local discontinuities in surfaces. At a first approximation, slowly adapting type 1 fibres respond to the depth of skin indentation, rapidly adapting fibres respond to the rate of skin indentation and Pacinian corpuscle-associated fibres respond to the acceleration of the skin[301]. The fourth type of nerve fibre, slowly adapting type 2 fibre, is thought to innervate Ruffini-like endings, which are located deep under the skin and respond to skin stretch. The responses of nerve fibres are highly precise and repeatable and are well captured by simple models that incorporate skin biomechanics and basic neuronal dynamics[301–303].

Proprioceptive signals originate primarily from mechanoreceptors embedded in the muscles and tendons, although cutaneous mechanoreceptors may also contribute[300]. Muscle spindles, which run parallel to muscle fibres, are the primary source of information about the conformation and movements of the body, whereas Golgi tendon organs, which run in series with the muscles (given their location in the tendons), are primarily responsible for conveying information about forces exerted by the muscles. Signals from both types of nerve fibre are integrated to achieve veridical representations of limb conformation and applied forces[304]. Nerve fibres that innervate the joints tend to respond only at the joint extrema, when the joint risks damage305_308, and are therefore poorly suited to convey postural information. However, a small proportion of hand joint afferents signal joint angle across the range of motion[309,310], although their role in proprioception has yet to be conclusively established.

Around 3,900 spindles populate hand-associated muscles (56 on average in intrinsic muscles and 184 in forearm-based muscles, estimated from REFs[311,312]) and approximately half as many Golgi tendon organs populate hand-associated tendons[313,314]. The idea that hand muscles are more densely innervated by spindles than are other muscles is appealing but not supported by the evidence[315]. Similarly, the density of motor units innervating hand muscles is comparable to its proximal limb counterpart[316–318]. However, because hand muscles tend to be smaller, and so their motor units less numerous, fluctuations in manually applied forces are relatively higher than for their proximal limb counterparts[319–322].

Signals from tactile and proprioceptive fibres that innervate the skin and muscles of the hand project to the cuneate nucleus in the brainstem, in some cases via spinal interneurons[323]. Cuneate neurons then project to the ventroposterolateral nucleus of the thalamus, which in turn projects to the primary somatosensory cortex, located on the postcentral gyrus, just posterior to M1. The somatosensory cortex is organized somatotopically, with adjacent neurons responding to stimulation of adjacent and well-defined body regions (FIG. 4). The somatosensory homunculus comprises four body maps, one each in Brodmann areas 3a, 3b, 1 and 2, which exhibit proprioceptive responses (area 3a), cutaneous responses (areas 3b and 1) or both (area 2). As is the case in M1, the sensory representation of the hand is magnified in the somatosensory cortex, accounting for more than 20% of its total surface area[223,324–326]. The hand representation comprises clearly delineated representations of each digit, separated by cell-poor septa[327], with the thumb located laterally (abutting the face representation) and the little finger medially (near the forearm representation). The thumb and index finger representations in area 3b are slightly enlarged relative to those of the other digits, particularly in adults[327].

Tactile coding of object interactions

Touch conveys precise information about contacts with objects to guide manipulation[328]. First, during reach and grasp, object contact gives rise to a strong phasic transient response throughout the somatosensory neuraxis[329], inherited from rapidly adapting nerve fibres and Pacinian corpuscle-associated nerve fibres, which triggers the end of the reach and the beginning of the grasp[330]. Abolition of touch, via digital anaesthesia for example, leads to slower movements, longer movement paths and a larger maximum finger aperture during reach to grasp[331]. Loss of touch also leads to decreased accuracy in reach-and-point tasks[332]. Second, when we transport an object, the forces we apply depend on the shape, frictional properties and mass of the object to prevent slip, typically exerting between 10% and 40% more force than is necessary, the ‘safety margin’[333–336]. When touch is abolished, our ability to adequately grade applied force is eliminated, leading to our dropping objects or exerting unnecessarily high forces[331,337]. Third, when a grasped object is subjected to an unexpected perturbation, tactile signals — particularly from rapidly adapting fibres — trigger an automatic grip adjustment before the perturbation reaches conscious access[299,338]. Fourth, touch conveys information about a change in the dynamics of a grasped object; for example, when it makes contact with another object[339]. When a grasped rod makes contact with an object, we can even sense the location of object contact along the rod on the basis of tactile signals[340].

The importance of touch in guiding manual behaviour is attested by the fact that caudal M1 — which predominantly drives hand movements — receives more tactile input and rostral M1 — which predominantly drives proximal limb movements — receives more proprioceptive input[341,342]. However, even for basic object interactions, proprioceptive information and tactile information are tightly coupled, as evidenced by the fact that reflexive grip adjustments triggered by cutaneous signals about object slip depend on the posture of the arm (reviewed in REF.[343]).

Tactile coding of object features

Object manipulation relies not only on tactile signals about contact events and applied forces but also on somatosensory signals about the objects themselves. When we grasp an object, we sense its texture and local geometry (edges, corners and surface curvature) by touch alone. If the object moves across our skin, the sense of touch conveys information about its movement direction and speed. These object-related signals support the manipulation of objects. For example, on the basis of the sensed edges of a mobile phone, we can operate it via the touchscreen without looking. Similarly, the sensed motion of a manipulated object can trigger an update of its position, which is critical for further manipulation. The transmission of this object information via the somatosensory system enables object interactions when vision is unavailable. Indeed, the absence of vision often has little impact on the ability to manipulate objects, as epitomized by the act of buttoning a shirt[344]. Even in the presence of vision, however, object manipulation benefits from somatosensory representations, which convey information about objects beyond that available visually. As alluded to earlier, tactile texture signals guide the application of grip force appropriate to the frictional properties of the texture[333–336]. Sensory signals related to other object features, such as edges and corners, also play a critical role in guiding hand–object interactions, but the behavioural role of these signals has not been investigated in a laboratory setting.

Sensory information about objects grasped in the hand is multiplexed in patterns of activation in tactile nerve fibres, where all classes of nerve fibres convey information about most object features[345]. Some features are encoded in the strength of the response, whereas others are encoded in its spatial and/or temporal patterns. These different neural codes allow a relatively small population of nerve fibres (~17,000) to simultaneously convey information about a variety of features — shape, motion and texture. Downstream neurons respond selectively to spatio-temporal features in the afferent input, and successive stages of processing — from the cuneate nucleus through to the cortex — culminate in explicit representations of behaviourally relevant features of contacted objects, including their shape, material, identity and motion across the skin. Accordingly, damage to cortical fields associated with somatosensation can lead to tactile agnosia, an inability to identify an object or recognize its shape or size[346–349].

Shape and coarse texture.—At each point of contact with an object, we sense its local geometric features — the presence of an edge, the curvature of a surface or millimetre-scale textural elements. These features are encoded in the spatial pattern of activation of tactile nerve fibres: the spatial configuration of the object's local features is reflected in the spatial pattern of activation it evokes in a subpopulation of nerve fibres[350–352] (FIG. 5a). Information about object features is extracted from this neural image by elementary feature detectors in the somatosensory cortex[353]. For example, a subpopulation of neurons in the somatosensory cortex exhibits a preference for edges at a specific orientation[354]. Higher-order tactile representations exhibit increasingly complex and invariant feature selectivity — for curved edges[355–357] or consistent orientation tuning over large swaths of skin[358], which is well suited to support object manipulation and recognition.

Motion.—When an object moves across the skin, we can sense both the direction in which it is moving and the speed at which it is moving[359–361]. In the somatosensory cortex, a subpopulation of neurons is tuned for the direction in which objects move across the skin[362–365]. While we can also sense the speed at which objects move across our skin, tactile speed perception is unreliable and strongly dependent on other properties of the moving object[361,442].

Texture.—As mentioned already, we can sense textures on submicron-level spatial scales, far beyond the spatial resolution of the skin, which is on the order of a millimetre given its innervation density[289]. To discern finely textured surfaces requires movement between skin and the surface[292,366], which leads to the elicitation of small, high-frequency, texture-specific vibrations in the skin[367–370]. In turn, these vibrations are transduced by Pacinian corpuscle-associated fibres, which are exquisitely sensitive to such skin vibrations and carry texture information in exquisitely precise temporal spiking patterns[371] (FIG. 5b). This temporal code is deciphered by downstream neurons that exhibit an idiosyncratic preference for a specific temporal feature in the afferent input[372,373]. The combination of the spatial and temporal coding mechanisms endows us with a sensitivity to texture over a wide range of spatial scales, ranging from tens of nanometres to tens of millimetres. As mentioned earlier, texture signals inform the grip forces deployed to grasp an object.

Proprioceptive coding

Hand use relies not only on a rich sense of touch — which conveys information about contact events and about object features at each point of contact — but also on a proprioceptive sense — which conveys information about the state of the hand, including its conformation, its movement and the forces it exerts on objects. Individuals deprived of proprioception rely heavily on vision to keep track of the current state of their hand and lose the ability to use their hands in the absence of vision[374].

Brodmann areas 3a and 2 of the somatosensory cortex contain neurons that respond to hand postures. In both areas, individual neurons track the time-varying angle of multiple joints — on average eight – distributed over the entire hand[135]. This postural representation of the hand stands in contrast with movement representations of the proximal limb in the somatosensory cortex, characterized by phasic responses during movement and weaker responses during maintained posture[375,376]. One possibility is that the postural representation of the hand reflects greater innervation of hand-related muscles by secondary spindle afferents, which preferentially encode muscle length, while movement representations of the arm reflect a preferential innervation of primary spindle afferents, which respond strongly to changes in muscle length[377,378]. Consistent with this hypothesis, sensitivity to changes in joint angle is greater than sensitivity to changes in joint angular velocity for the hand, but the reverse is true for the arm[379]. Another possibility is that the differences between postural representations of the hand and movement representation of the arm reflect differences in the biomechanics — the hand being much lighter than the arm — as mentioned in the context of M1 coding. Regardless, the proprioceptive representation of the hand is well suited to encode hand conformation, whereas the proprioceptive representation of the arm is better suited to encode speed[380].

Open questions

Although some of the specialized neural circuits for control and sensing that mediate dexterity have been identified, several major aspects of manual behaviour are poorly understood. First, we are endowed with the ability to precisely regulate the force we exert on objects with our hands, an ability that relies on dozens of muscles in the hand and forearm. The precision of force regulation has been documented only for simple behaviours — grasping or pushing[27,381] — but many manual behaviours require regulating forces across fingers in a more individuated fashion. Virtually nothing is known about how manual forces are encoded in the responses of neurons in the motor cortex or the somatosensory cortex[152,376,382,383].

Second, when we grasp an object, we experience a vivid sense of its three-dimensional structure based solely on signals stemming from the hand, an ability, termed ‘stereognosis’, that involves the integration of tactile and proprioceptive signals: at each point of contact with the object, cutaneous signals convey information about the object’s local geometry (for example, the presence and orientation of an edge or the curvature of a surface). These cutaneous signals about local geometric features are then integrated with proprioceptive signals about the locations of the contact points relative to one another in space. Cutaneous signals from the glabrous skin, a uniquely deformable sensory sheet, must be interpreted in the context of its conformation, conveyed by proprioceptive signals. Very little is known about how tactile signals are integrated with proprioceptive ones, except that this integration begins to take place in Brodmann area 2 (REF.[384]), or about how this integrated neural representation gives rise to stereognosis. The ability to sense the three-dimensional structure of an object is probably critical to our ability to manipulate objects dexterously. Indeed, our ability to deftly manipulate objects without the guidance of vision implies an object representation that can be updated via somatosensory signals alone.

Third, large swaths of the sensorimotor apparatus are only beginning to receive experimental attention in the context of dexterous manual behaviour, including the cerebellum[385–389], the reticulospinal pathway[390–393] and the spinal cord[186,394–396], even though damage to any of these structures and pathways leads to severe motor deficits that permanently affect manual dexterity. These structures and pathways are liable to have developed hand-related specializations that parallel the various specializations described above.

Fourth, the mechanisms of motor learning have been extensively studied in the context of simple behaviours[397–405], but learning a highly dexterous behaviour — playing a musical instrument, writing or drawing — may entail additional and heretofore unknown mechanisms of learning.

Conclusions

Manual dexterity reflects the confluence of many physiological factors, which we are only beginning to uncover. The many bones of the hand confer on it a wide space of achievable postures, and the numerous muscles that articulate the joints allow constrained individuation and remarkable strength. In the peripheral nervous system and CNS, sensorimotor representations of the hand are outsized to support the hand's versatility and precision. On the motor side, a monosynaptic pathway between the motor cortex and motor neurons provides the CNS with a privileged access to the muscles. On the sensory side, a multitude of nerve fibres innervate the skin and muscles of the hand to convey high-resolution feedback not only about manual interactions with objects but also about the objects themselves. These sensory signals are critical to hand use and cannot be replaced with other senses. The relative contributions of the different sensorimotor pathways to dexterity remain to be disentangled, and the integration of somatosensory signals remains poorly understood. However, the evidence suggests that the versatility and precision of the hand is mediated by distinct biomechanical and neural mechanisms supplementing the systems controlling non-dexterous behaviour.

With recent technological developments in hand tracking and sensor technology, we are poised to address these and other gaps in our understanding of hand control. Manual behaviour epitomizes the ability of the nervous system to produce complex outputs. Glimpses into the neural mechanisms of dexterity will yield insights into the unique ability of nervous systems to give rise to flexible, intelligent behaviour and guide the development of ever more dexterous bionic hands (BOX 2).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Degrees of freedom

In the context of limbs, the axes of rotation of one segment around another segment. A single joint can have multiple degrees of freedom, each corresponding to a different axis of rotation.

Metacarpals

Bones that underlie the primate palm, one for each digit.

Metacarpophalangeal joints

Joints that connect metacarpal bones of the palm with the first phalanx.

Prehension

The act of seizing or grasping.

Interphalangeal joints

Joints that connect two phalanges of a digit.

Torques

In the context of limbs, the rotational forces around a joint.

Contralateral

Located on the opposite side of the body.

Hemiparesis

Weakness of voluntary movement in one side of the body.

Pyramidal neurons

Large excitatory neurons in the cortex.

Motor neuron

A neuron that directly synapses onto muscles.

Spinal reflexes

Semi-automatic neural circuits connecting peripheral sensors to motor neurons via one synapse or several synapses in the spinal cord.

Mechanoreceptors

Sensory receptors that convert mechanical deformations into electrochemical neural signals.

Glabrous skin

Hairless skin, such as that on the palmar side of the hand.

Brodmann areas

Areas of the cerebral cortex defined by their cell composition, structure and organization.

Somatosensation

The sense of one’s own body, including the sense of touch, the sense of the posture and movements of the body (proprioception), the sense of temperature (thermosensation) and the perception of pain (nociception).

Tetraplegia

Paralysis of all four limbs.

BOX 1 |

Rodent hands

Rodents are a popular model to study motor control[406–410]. Although the hand and arm musculature of rodents is grossly similar to that of primates, it differs in a number of ways[98]. First, superficial and deep finger flexors are not as well separated. Second, intrinsic hand muscles have vastly different anatomy. Third, rats have fewer muscles to articulate their (diminutive) thumbs. The rodent wrist also has fewer degrees of articulation because of fused bones[46]. By contrast, rats have as many little finger muscles as primates, reflecting the importance of this digit for grasping small objects[407].

Rodents adjust hand aperture on the basis of the size of an object and can perform one-handed grasps, but object manipulations typically involve both hands and the mouth and are often performed without visual guidance[406,410,411]. Some level of finger individuation (mostly of the little finger) is observed when the hand approaches a food pellet[408] but much less so than is measured in primates[24,135]. Furthermore, the success rate of prehension is usually much lower for rodents (~40–50%) than primates, even after extensive training.

BOX 2 |

Bionic hands

one of the great achievements of the twenty-first century is the development of devices that allow humans not only to volitionally control extracorporeal devices such as robotic limbs by thought alone but also to actually feel through them. These feats are made possible by chronic electrical interfaces with the nervous system. For individuals with amputations, intended movements are inferred from patterns of activation of residual muscles and sensory feedback is delivered by electrically stimulating the residual nerves that innervated the amputated limb before the injury[412–418]. For individuals with tetraplegia, movement intent is inferred from patterns of activation across populations of cortical neurons, typically in the primary motor cortex but sometimes in the posterior parietal cortex, and sensory feedback is delivered by electrically stimulating neurons in the somatosensory cortex[419–427].

Given the staggering complexity of the human hand, it should come as no surprise that robotic hands are far simpler in their actuation and sensitization than their biological counterparts. The most sophisticated bionic hands feature around 20 degrees of freedom[428,429] and a handful of sensors on the fingertips, which convey only coarse information about contact with objects. Although better sensorization is just around the corner[430–432], the main bottleneck is not the impoverished sensory feedback but the inadequacy of the control signals. Indeed, myoelectrically controlled bionic hands suffer from the fact that many of the muscles relevant to hand use (including all the intrinsic hand muscles) are missing in people with amputations, which severely limits the reliability of the resulting control[418]. Brain-controlled bionic hands are limited by an insufficient understanding of the neural mechanisms underlying manual control. Successful brain control, which has focused on proximal limb movements designed to place the hand in peripersonal space, has achieved limited manual control — often including only hand opening and closing — and relies completely on kinematic decoding from the motor cortex[423]. That is, the individual closes the hand into the object rather than volitionally exerting a force on it, as we naturally do. Nonetheless, state-of-the-art brain–machine interfaces have achieved control of an anthropomorphic robotic limb across ten degrees of freedom[433] and conveyed intracortical microstimulation-based tactile feedback that conferred additional dexterity on the device[434].

Next-generation brain-controlled bionic hands will allow manual control of forces over many degrees of freedom. For individuals with amputations, improved control may have to rely on a combination of myoelectric and efferent neural signals monitored in the residual nerves[418,435]. For individuals with tetraplegia, hybrid kinematic and force control for the hand will require a more detailed understanding of hand representations in the primary motor cortex. Work with myoelectrically controlled bionic hands has shown that biomimetic sensory feedback — designed to mimic natural signals in the nerve through electrical stimulation[436,437] — leads to improved performance compared with standard sensory feedback, which simply tracks the output of force sensors on the bionic fingers[438,439]. Intracortical microstimulation-based biomimetic sensory feedback is also likely to lead to improved performance over standard algorithms, but this has yet to be tested[440,441].

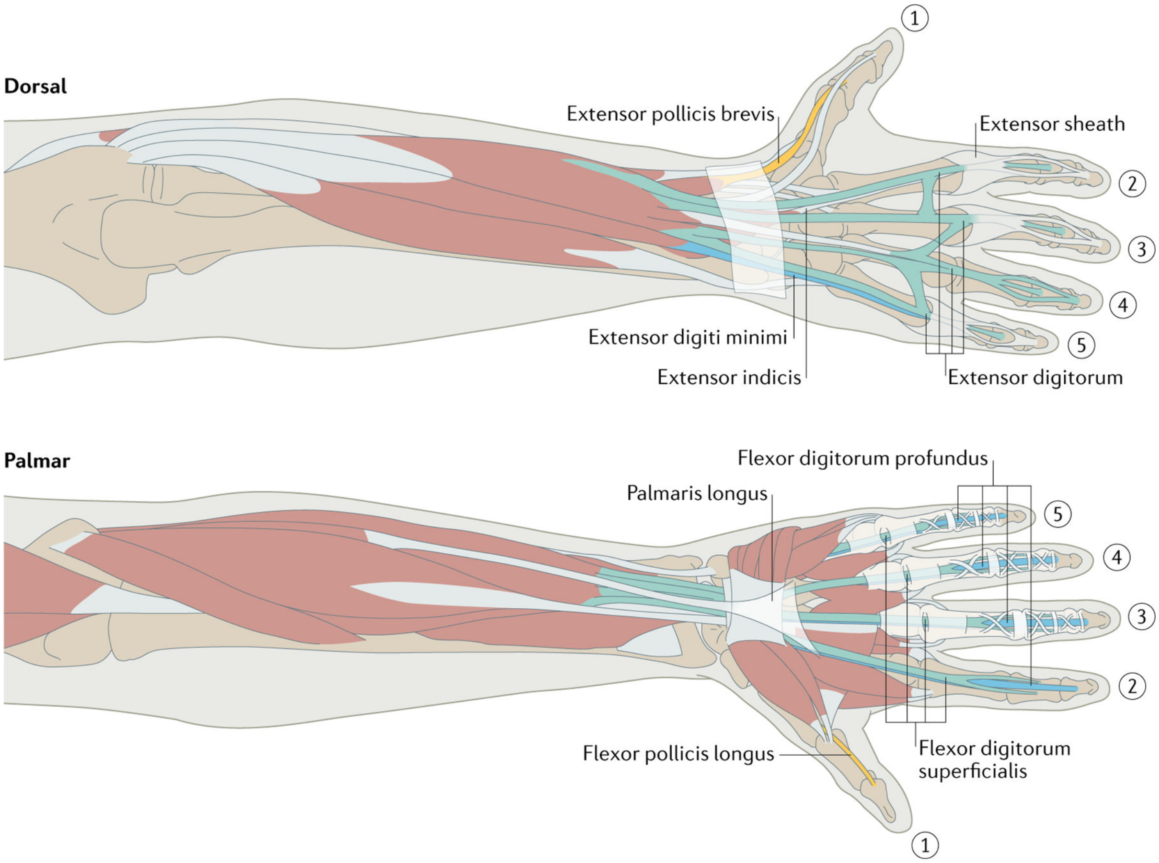

Fig. 1 |. Hand musculature.

Digits 2–5 are articulated mainly by two flexors — note how the deep one (blue) threads through the superficial one (green) at the proximal phalanx — and one extensor, which feeds into the extensor sheath. Intrinsic hand muscles also feed into the sheath, flexing the proximal finger joint and extending the other. Extensor indicis and extensor digiti minimi contribute further independence to index finger and little finger extension. Flexor pollicis longus and extensor pollicis brevis are two thumb muscles that are found only in humans and two other primate species. Palmaris longus lies outside the carpal tunnel and is absent in many people. Each muscle path is complex, especially around the wrist and thumb, wrapping around other moving muscles and bones, so estimating the action of these muscles is difficult. Some hand muscles and other tissues are omitted for clarity. In addition, the extensor sheath is omitted on the dorsal view of digit 4 and the connective tissue is omitted on the palmar view of digit 2 to reveal the underlying tendon paths. Image courtesy of Kenzie Green.

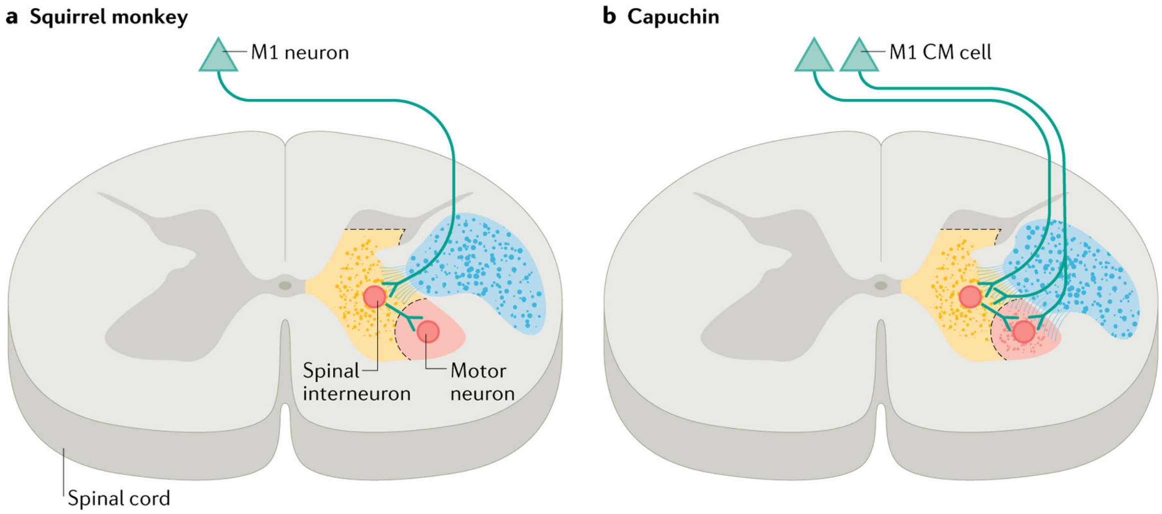

Fig. 2 |. Direct and indirect pathways from the cortex to the muscles.

Traced axons (dots) from the primary motor cortex at the C8 level of the spinal cord. **a** | Such tracing has revealed that, in squirrel monkeys, neurons from the primary motor cortex (M1) project via the pyramidal tracts (blue region) to spinal interneurons (located in the yellow region), which in turn project to motor neurons (located in the red region). **b** | In capuchins, M1 sends direct projections to motor neurons in addition to indirect projections through spinal interneurons. Presumably owing in part to this direct pathway, capuchins are more dexterous than squirrel monkeys. CM, corticomotoneuronal. Adapted with permission from REF.[204], Copyright 1993 Society for Neuroscience.

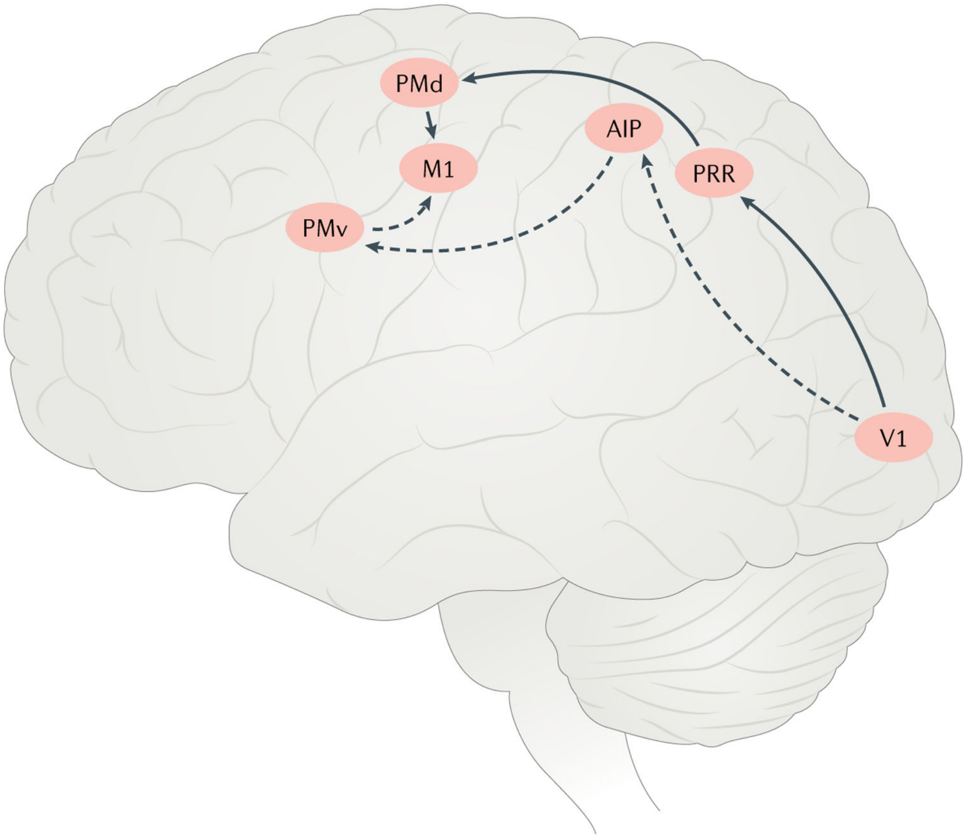

Fig. 3 |. Main cortical regions and pathways involved in visuomotor control of the hand.
Visual information from the primary visual cortex (V1) is transformed in the parietal reach region (PRR) to guide reaching movements via the dorsal premotor area (PMd). Similarly, the anterior interparietal area (AIP) processes visual information about object shape to guide grasping movements via the ventral premotor area (PMv). The PMv and the PMd both project to the primary motor cortex (M1).

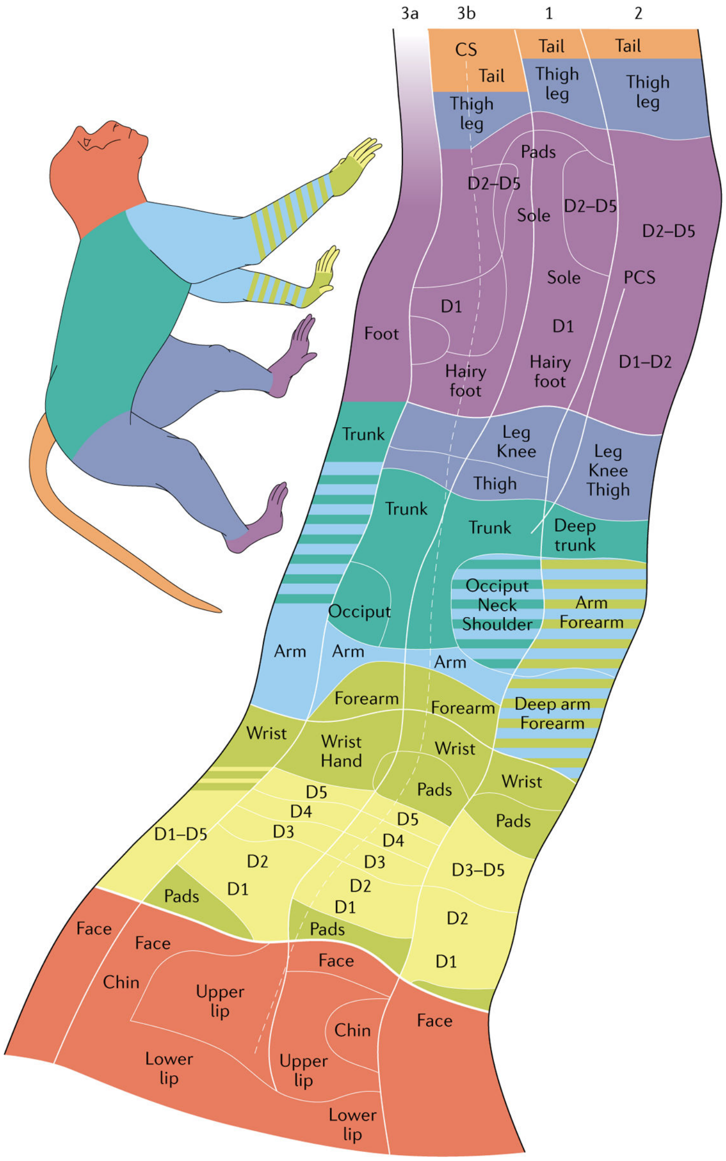

Fig. 4 |. Body maps in the somatosensory cortex of a monkey.

Touch applied to a location on the body activates a spatially restricted population of neurons in the somatosensory cortex. Nearby neurons are activated by nearby patches of skin, leading to highly structured maps of the body, termed the ‘somatosensory homunculus’. In primates, the volume of the cortex devoted to the hand is very large. Within this volume, the neural representations of individual digits are spatially distinct. CS, central sulcus; D, digit; PCS, postcentral sulcus. Adapted with permission from REF.[326], Wiley.

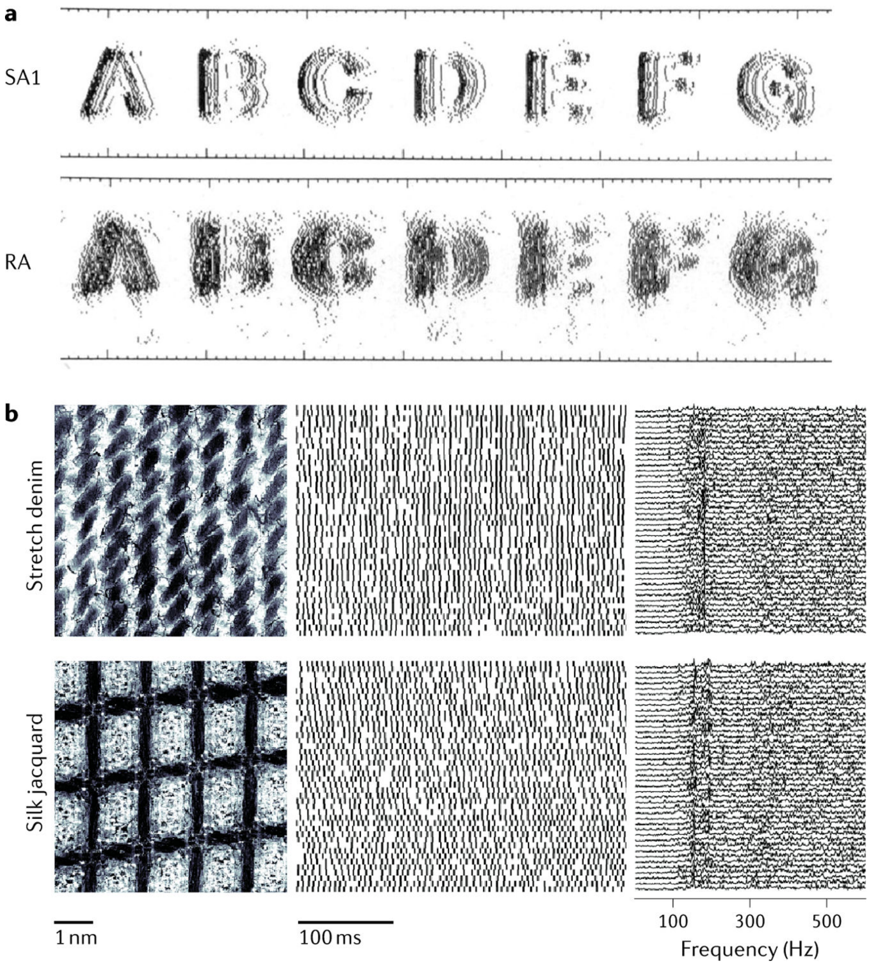

Fig. 5 |. Neural coding of touch.

a | Reconstructed response of a population of slowly adapting type 1 (SA1) fibres and rapidly adapting (RA) fibres when embossed letters are scanned across the fingertip. The spatial pattern of activation in SA1 fibres and to a lesser extent in RA fibres carries a faithful representation of the stimulus. **b** | Responses of a Pacinian corpuscle-associated fibre (middle) to 40 repeated presentations of two textures (left) scanned across the skin. As shown in the spectrogram of the response (right), Pacinian corpuscle-associated fibres produce highly repeatable spiking patterns that differ across textures. This temporal code conveys information about fine texture. Part **a** adapted with permission from REF.[350], PNAS. Part **b** adapted with permission from REF.[371], PNAS.