

# Coding and use of tactile signals from the fingertips in object manipulation tasks

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**Abstract** | During object manipulation tasks, the brain selects and implements action-phase controllers that use sensory predictions and afferent signals to tailor motor output to the physical properties of the objects involved. Analysis of signals in tactile afferent neurons and central processes in humans reveals how contact events are encoded and used to monitor and update task performance.

## Tactile afferents

Fast-conducting myelinated afferent neurons that convey signals to the brain from low-threshold mechanoreceptors in body areas that actively contact objects — that is, the inside of the hand, the sole of the foot, the lips, the tongue and the oral mucosa.

## Proprioceptive afferents

Fast-conducting myelinated afferents that provide information about joint configurations and muscle states. These include mechanoreceptive afferents from the hairy skin, muscles, joints and connective tissues.

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doi: 10.1038/nrn2621

Published online 8 April 2009

The tactile afferents that innervate the inside of the hand signal the transformation of soft tissues that occurs when the hand interacts with objects and thus provide information about the physical properties of the object and the contact between the object and the hand. People with impaired tactile sensibility have difficulties with many everyday activities because the brain lacks the information about mechanical contact states that is needed to plan and control object manipulations. Vision provides only indirect information about such mechanical interactions, and proprioceptive afferents exhibit low sensitivity to mechanical fingertip events<sup>1–4</sup>.

In this Review, we address emerging concepts regarding the use of tactile information by the brain in manipulation tasks. In doing so, we discuss the notion that the planning and control of manipulation tasks is centred on mechanical events that mark transitions between consecutive action phases and that represent subgoals of the overall task. We highlight recent findings that help explain the speed with which the brain detects and classifies tactile fingertip events in object manipulation. Finally, we discuss multisensory representation of action goals in object manipulation. Our account differs from a recent review of tactile signals in manipulation<sup>5</sup> by emphasizing the use of these signals in the control of manipulatory tasks, by considering how other sensory signals contribute to this control and by discussing the central neural mechanisms involved in manipulation tasks.

## Tactile sensors encoding fingertip transformations

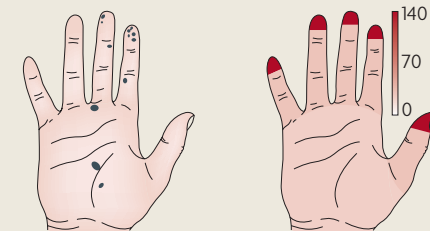
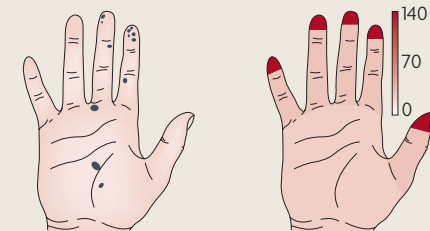
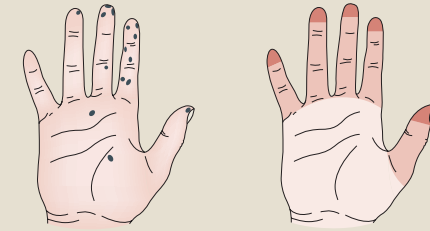
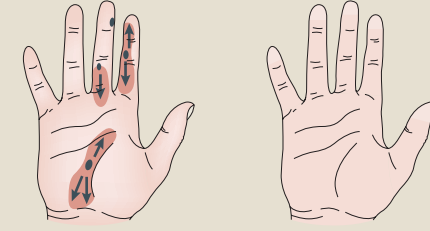
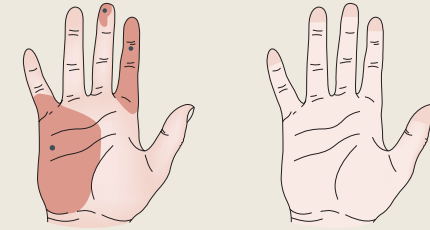
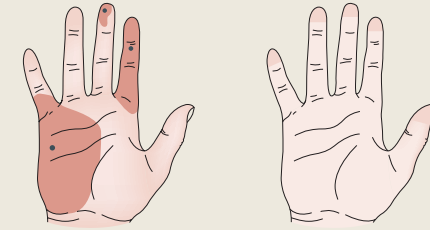
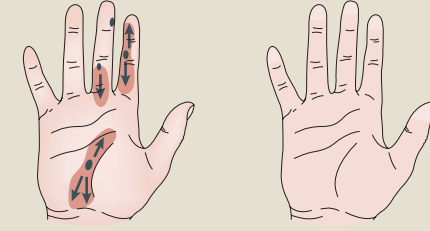
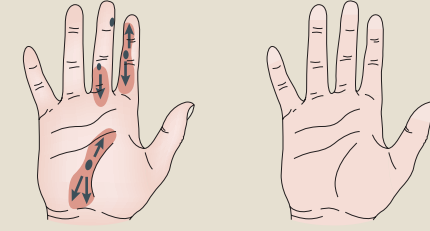
When humans manipulate objects, the brain uses tactile afferent information related to the time course, magnitude, direction and spatial distribution of contact forces, the shapes of contacted surfaces, and the friction between contacted surfaces and the digits. The inside of

the human hand is equipped with four functionally distinct types of tactile afferents (TABLE 1; reviewed in more detail in REFS 5,6). FA-I (fast-adapting type I) and SA-I (slow-adapting type I) afferents terminate superficially in the skin, with a particularly high density in the fingertips. FA-Is exhibit sensitivity to dynamic skin deformations of relatively high frequency<sup>7,8</sup>, whereas SA-Is are most easily excited by lower-frequency skin deformations<sup>7,8</sup> and can respond to sustained deformation. There are more FA-I afferents than SA-I afferents in the fingertips (TABLE 1), reflecting the importance of extracting spatial features of dynamic mechanical events, such as the skin forming and breaking contact with objects or scanning across a textured surface.

FA-II and SA-II afferents innervate the hand with a lower and roughly uniform density and terminate deeper in dermal and subdermal fibrous tissues. FA-II afferents are optimized for detecting transient mechanical events<sup>7–10</sup>. Hundreds of FA-II afferents, distributed throughout the hand, can be excited when hand-held objects contact or break contact with other objects<sup>11</sup>. SA-II afferents can respond to remotely applied lateral stretching of the skin<sup>12,13</sup> and can be sensitive to the tangential shear strain to the skin that occurs during object manipulation<sup>2,11</sup>. SA-II-like afferents are found in most fibrous tissues (such as muscle fascias and joint capsules and ligaments)<sup>14</sup> and there is evidence that they can act as proprioceptors (BOX 1).

Traditional studies on tactile sensing that examine correlations between afferent signals and perceptual (declarative) phenomena evoked by gently touching passive digits (for reviews see REFS 6,14–20) provide little information about the encoding and use of tactile information in object manipulation for several reasons: the control processes that are active in manipulation operate

Table 1 | **Tactile sensory innervation of the hand**

Afferent type (and response properties)	Receptive field (and probe)	Density (afferents per cm <sup>2</sup> )
<b>FA-I (fast-adapting type I)</b> Meissner endings <ul style="list-style-type: none"> <li>• Sensitive to dynamic skin deformation of relatively high frequency (~5–50 Hz)</li> <li>• Insensitive to static force</li> <li>• Transmit enhanced representations of local spatial discontinuities (e.g., edge contours and Braille-like stimuli)</li> </ul>		
<b>SA-I (slowly-adapting type I)</b> Merkel endings <ul style="list-style-type: none"> <li>• Sensitive to low-frequency dynamic skin deformations (&lt;~5 Hz)</li> <li>• Sensitive to static force</li> <li>• Transmit enhanced representations of local spatial discontinuities</li> </ul>		
<b>FA-II (fast-adapting type II)</b> Pacini ending <ul style="list-style-type: none"> <li>• Extremely sensitive to mechanical transients and high-frequency vibrations (~40–400 Hz) propagating through tissues</li> <li>• Insensitive to static force</li> <li>• Respond to distant events acting on hand-held objects</li> </ul>		
<b>SA-II (slowly-adapting type II)</b> Ruffini-like endings <ul style="list-style-type: none"> <li>• Low dynamic sensitivity</li> <li>• Sensitive to static force</li> <li>• Sense tension in dermal and subcutaneous collagenous fibre strands</li> <li>• Can fire in the absence of externally applied stimulation and respond to remotely applied stretching of the skin</li> </ul>		

Data from REFS 6,20.

## Action-phase controller

A learned sensorimotor 'control policy' that uses specific sensory information and sensory predictions to generate motor commands to attain a sensory goal.

## Sensorimotor control point

A planned contact event in which predicted and actual sensory signals are compared to assess the outcome of an executed action-phase controller.

largely subconsciously and very rapidly, the use of tactile signals differs across tasks and task phases, and the forces that are involved in manipulation typically differ from the forces that are present during gentle touch.

The information that a mechanoreceptive afferent conveys depends on several factors, including the branching of the nerve terminal, the mechanical properties of the end organs of the nerve endings, the anchoring of the end organs in the surrounding tissues and, not least, the overall mechanical deformational properties of these tissues. Thus, the distributed patterns of stresses and strains that develop in the skin and the underlying tissues when a fingertip interacts with an object affect both afferents that terminate in contact areas and afferents that terminate remotely<sup>21–23</sup>. This implies that the

actual receptive field of an afferent can be considerably larger than the classical cutaneous receptive field delineated by lightly touching the hand with a pointed object (TABLE 1). Consequently, models of neural encoding of tactile stimuli that visualize the receptor mosaic as a two-dimensional pixel-like array of densely localized sensors distributed over a flat skin surface<sup>15–17</sup> are not viable for predicting tactile signalling in manipulation tasks. Importantly, the functional overlap of large receptive fields can enhance rather than degrade the encoding of spatiotemporal information<sup>24,25</sup>.

Owing to the mechanical properties of the fingertip, the mapping between fingertip events and afferent responses is highly complex<sup>16,22,23</sup>. Simply looking at how the pattern of stress develops in the contact area when the fingertip contacts a flat surface demonstrates this complexity (BOX 2). Researchers have attempted to model the mechanics of the fingertip while incorporating its composite material properties, with the goal of predicting the responses of populations of tactile afferents to various fingertip stimuli<sup>26–34</sup>. However, no model yet possesses the level of realism that satisfies this goal.

## Contact events and action goals in manipulation

Dexterous manipulation tasks can be broken down into a series of action phases, usually delimited by the mechanical events that represent subgoals of the task (see REFS 5,35 for details). For example, when picking up a hammer to strike a nail, contact between the digits and the handle marks the end of the reach phase; the braking of contact between the hammer and the support surface marks the end of the load phase; and contact between the hammer head and the nail marks the end of the swing phase. Mechanical events involved in manipulation generate specific patterns of activity in the tactile afferents and often also in auditory and visual afferents. Thus, manipulation tasks can be specified as a sequence of specific sensory events linked to subgoals.

To achieve these subgoals the brain has to select and execute appropriate action-phase controllers<sup>5</sup> (BOX 3). In order to accurately predict the required motor output and associated sensory events, action-phase controllers must have information about the properties of the objects involved and the current state of the motor apparatus. If predictions are erroneous, corrective actions can be launched based on real-time sensory information. However, because of the long time delays in sensorimotor control loops engaged in corrective actions (~100 ms), dexterous manipulation is not possible unless predictions are accurate<sup>5</sup>. In order to smoothly link action phases, the predicted terminal sensory state of the active controller could be used as the initial state by the controller responsible for the next action phase. If the brain relied on peripheral afferent information to obtain this state information, stuttering phase transitions would occur.

The comparison of predicted and actual sensory signals can be used to monitor task progression and detect performance errors (BOX 3). Contact events, which denote completion of action goals, represent crucial sensorimotor control points because they give rise to discrete sensory signals in one or more modalities. If an error is detected,

### Box 1 | Cutaneous afferents contribute to proprioception

Proprioception depends on both central<sup>217</sup> and peripheral signals. In the 1960s it was generally thought that the latter were provided through afferents from joints<sup>218,219</sup>, and in the 1970s the focus shifted almost exclusively to muscle spindles<sup>220,221</sup>. However, recent microneurography studies in humans have demonstrated a role for cutaneous mechanoreceptors as well, which faithfully signal strain patterns in the skin that change during movement. In contrast to tactile afferents, which supply glabrous (hairless) skin areas, cutaneous afferents in hairy skin, which is more elastic and more loosely anchored to supporting tissues, can respond vigorously to changes in skin strain during movements of adjacent joints. This applies to hairy skin on the face<sup>222</sup>, the back of the hand<sup>223–226</sup> and the lower limb<sup>227,228</sup>. Analyses of static and dynamic sensitivity indicate that cutaneous afferents are at least as sensitive to joint angle changes as muscle spindles are<sup>224,226</sup>. The quantitative properties of SA-II (slow-adapting type II) afferents are most suited to encode joint configurations, but those of SA-III afferents (a receptor class that is present only in the hairy skin<sup>227</sup>) are a close second. The finding that skin stretching can produce movement illusions demonstrates that cutaneous signals contribute to kinaesthesia<sup>229–232</sup>.

corrective actions can be implemented. The nature of the correction is specific to the sensory signals, the controller and the current state of the system and environment. Furthermore, if errors occur, memory representations of object properties can be updated to improve subsequent predictive control.

The context-dependent nature of corrective responses is reminiscent of finite-state control systems that operate by implementing rules based on IF, AND and THEN arguments. Such systems have been used to model the control of phase transitions<sup>36</sup> and corrective actions<sup>37</sup> during walking. For example, the transition from the stance phase to the swing phase has been modelled with the following rules: IF the extensor force is low AND the hip is extended AND the contralateral leg is loaded, THEN flex<sup>36</sup>. Key concepts of finite-state control are that multiple sensory inputs are evaluated continuously to judge the state of the rules and that different states can give rise to different motor outputs. Furthermore, the rules and the weighting of sensory inputs can be adapted based on the anticipated state of the system. Task- and phase-specific use of sensory information in object manipulation is presumably acquired when we learn the underlying basic action-phase controllers, which occurs gradually during development<sup>38–43</sup>.

### Representation of action goals in tactile afferents

**Grasp contact.** Often the first goal in manipulation tasks is to ensure a stable grasp of the object<sup>44–48</sup>. Because of the low stiffness of the fingertip at low contact forces<sup>11,49</sup>, its shape transforms briskly when an object is initially contacted (BOX 2). Contact responses, especially in FA-I afferents but also in SA-I and FA-II afferents, provide information about the outcome of the reach phase<sup>11</sup> (BOX 3). Similar responses occur at the end of the unload phase when the digit breaks contact with the object.

For each digit, ensembles of afferents convey information about contact timing, the contact site on the digit and the direction of the contact force (BOX 3). The spatial centre of the afferent population response is related to the primary contact site on the finger<sup>50</sup>, whereas the recruitment of afferents and their firing rates reflect force intensity<sup>2,12,16,51,52</sup>. The firing rates of individual

tactile afferents are each broadly tuned to a preferred direction of contact force, allowing patterns of activity in ensembles of afferents to provide information on force direction<sup>22</sup> (FIG. 1a).

Contact events between digits and objects provide sensorimotor control points for the reach-phase controller. Behavioural studies indicate that this information is important for monitoring the accuracy of reach commands and making necessary adjustments in future reaches<sup>53–58</sup>. Disturbances of the contralateral primary sensorimotor cortex by weak single-pulse transcranial magnetic stimulation (TMS) delivered just before contact<sup>59</sup> or by TMS-induced ‘virtual lesions’ (REF. 60) delay the implementation of the subsequent load-phase controller, presumably because of disturbed processing of tactile afferent information and/or sensory predictions. Similar but smaller delays arise with TMS perturbations of the left anterior intraparietal area<sup>61</sup> and the left dorsal premotor cortex<sup>62</sup>, suggesting that these areas are also involved in processing tactile information for object manipulation.

**Grasp stability.** Once they are in contact with an object, the digits usually apply tangential forces to its surfaces in order to move and manipulate it (for example, load forces in order to lift an object). To ensure grasp stability they also apply grip forces normal (perpendicular) to the surfaces: these change in phase with, and proportional to, the applied tangential loads<sup>63–79</sup> (BOX 3). The control of grip forces is based on predictions of objects’ dynamical properties that influence the mapping between arm motor commands and resultant tangential forces and torques<sup>72,75,80,81</sup>.

Dexterous manipulation involves adapting the balance between grip and load forces to object surface properties, a capacity that is lost with impaired digital sensibility<sup>63,82–89</sup>. Healthy people adapt the balance between grip and load forces to different frictional conditions, using stronger grip forces with more slippery surfaces<sup>63,67,90</sup>. In fact, the local frictional conditions can tailor the grip-to-load force ratios at individual digits<sup>91–95</sup>. Similarly, people adjust grip and load forces to the shape of the object in order to ensure grasp stability<sup>64,83,84</sup>. As a result of these adaptations, excessive grip force is avoided: grip forces are normally 10–40% greater than the minimum required to prevent slips.

The initial contact responses in tactile afferents provide information about surface properties, which can be compared with predictions based on visual cues and/or sensorimotor memory (BOX 3 and see below). A mismatch between predicted and actual sensory information can trigger corrective actions leading to changes in grip-to-load force ratios commencing ~100 ms after contact and to an updating of the representation of the surface properties that is used in future interactions with the object (see REF. 5 for further details). Visual cues about the shape of the object can provide the information required to make these predictions<sup>83,84</sup>. However, shape information provided by tactile signals after contact can override predictions based on visual cues.

Evidence indicates that it is the responses of FA-I afferents to initial contact that are most important for

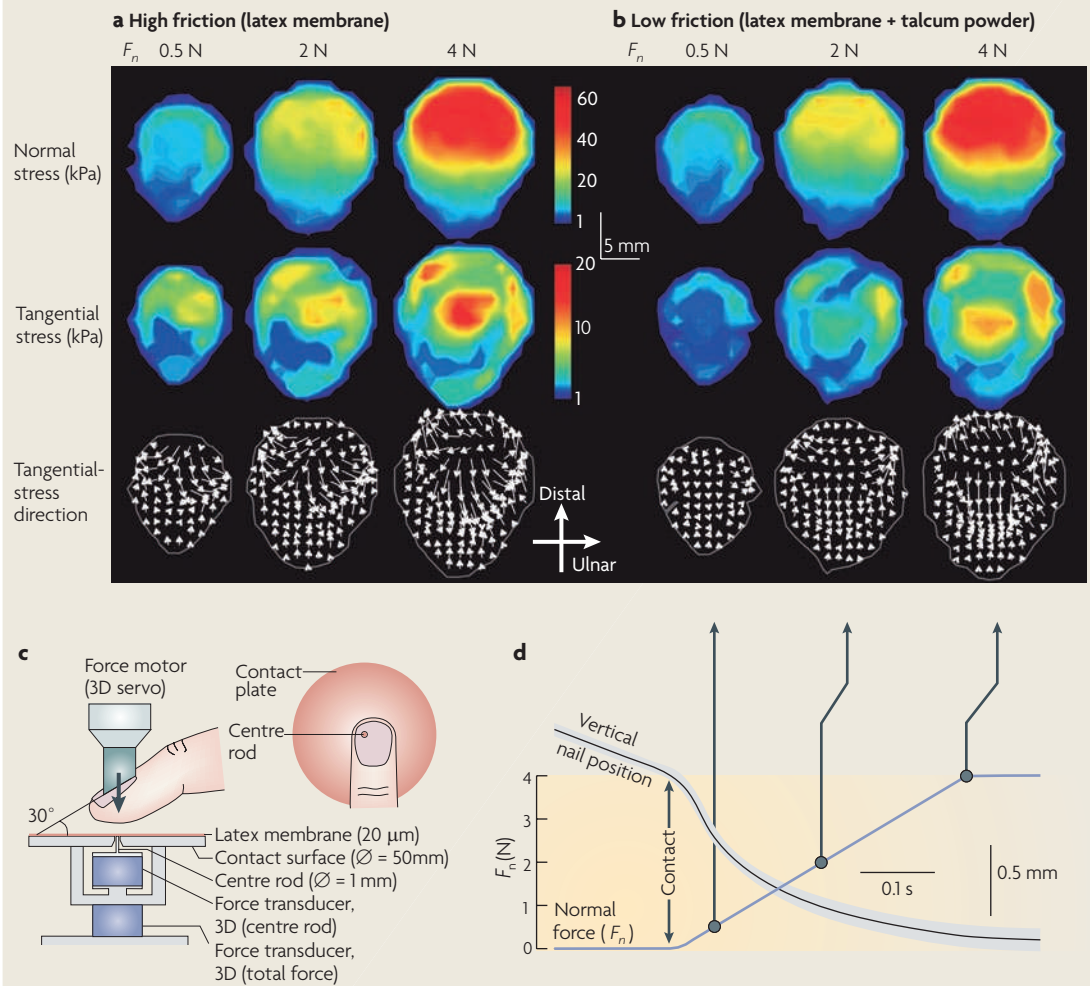
### Transcranial magnetic stimulation

(TMS). A non-invasive technique that can be used to induce a transient interruption of normal activity in a restricted area of the brain. It is based on the generation of a magnetic pulse near the area of interest that induces small eddy currents that stimulate neurons.

### Grasp stability

The control of grip forces such that they are adequate to prevent accidental slips but not so large that they cause unnecessary fatigue or damage to the object or hand.

Box 2 | Complex mechanical properties of the fingertip



The development of the pattern of stress in the contact area when the fingertip applies a normal (perpendicular) force to a flat surface illustrates the fingertip's complex deformational properties. The 'fingerprints' in part **a** of the figure illustrate the distributions of normal and tangential stresses when the fingertip contacts a stationary surface at three different normal force levels ( $F_n$ ). Part **b** shows corresponding stresses after the surface was made more slippery. Contact with the more slippery surface results in lower overall tangential stress because of lower frictional forces. That is, there is more localized frictional slipping and creeping in the contact area with the more slippery surface. Such slip and creep events constitute the basis for frictional encoding by tactile afferents: a slippery contact generally excites FA-I (fast-adapting type I) afferents more strongly than a less slippery contact<sup>96</sup>. These principles agree with recent mechanical models of shear strain and stress distributions in the contact area and with the observation that friction between a planar surface and an artificial finger can be estimated simply by pressing the finger against the surface<sup>34</sup>. Local normal and tangential stresses in parts **a** and **b** were measured through a thin rod located in the centre of, and flush with, a flat contact surface (**c**). A three-dimensional (3D) servomechanism (servo)<sup>22</sup> repeatedly moved the fingertip to make it contact the plate. For each movement,  $F_n$  was servo-controlled to increase linearly to 4 N, whereas the net force applied tangentially to the contact surface was servo-controlled at 0 N. By shifting the horizontal position of the contact surface and the attached transducers between movements, the distribution of normal and shear stresses in the contact area was mapped at 1 mm spatial resolution. As demonstrated by the position of the fingernail during normal force application (**d**), the vertical stiffness of the fingertip increases with the contact force.

encoding the amount of friction between fingertips and object surfaces<sup>96</sup>. A slippery contact tends to excite FA-I afferents more strongly than a less slippery contact (BOX 2). Most studies that have examined shape encoding by tactile afferents have used stimuli that generate small localized skin deformations and engage relatively few afferents in the immediate area of contact<sup>15,16,97–102</sup>.

By contrast, manipulation of everyday objects engages afferents all over the fingertip. Accordingly, the curvature of such objects influences firing rates in most FA-I, SA-I and SA-II afferents in the fingertips, and patterns of firing in ensembles of tactile afferents can provide information on curvature<sup>23</sup> (FIG. 1b). SA-II afferents probably provide coarser information about object shape and contact



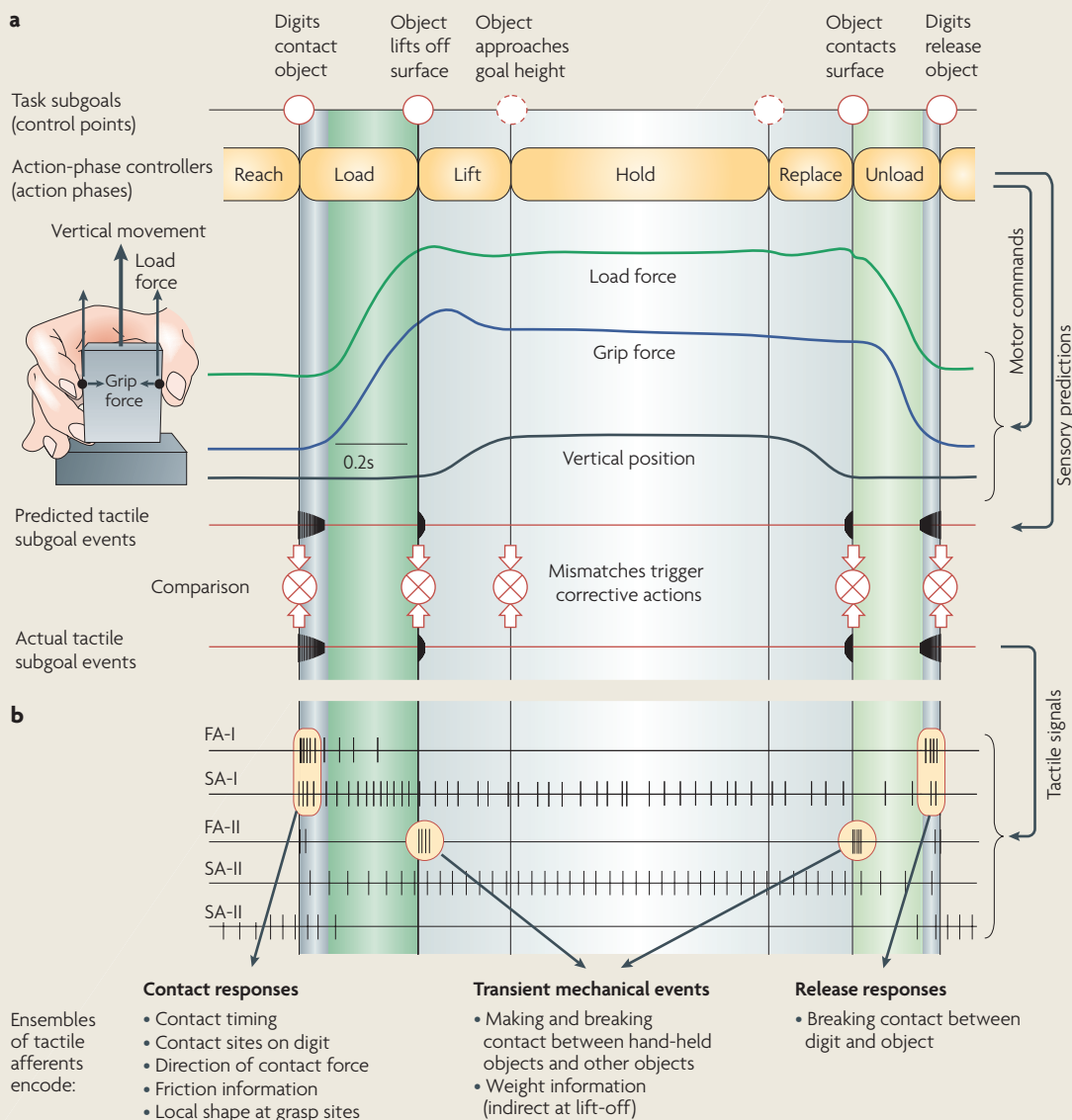
forces than the SA-I or the FA-I populations, because they innervate the fingertip more sparsely<sup>103</sup> (TABLE 1).

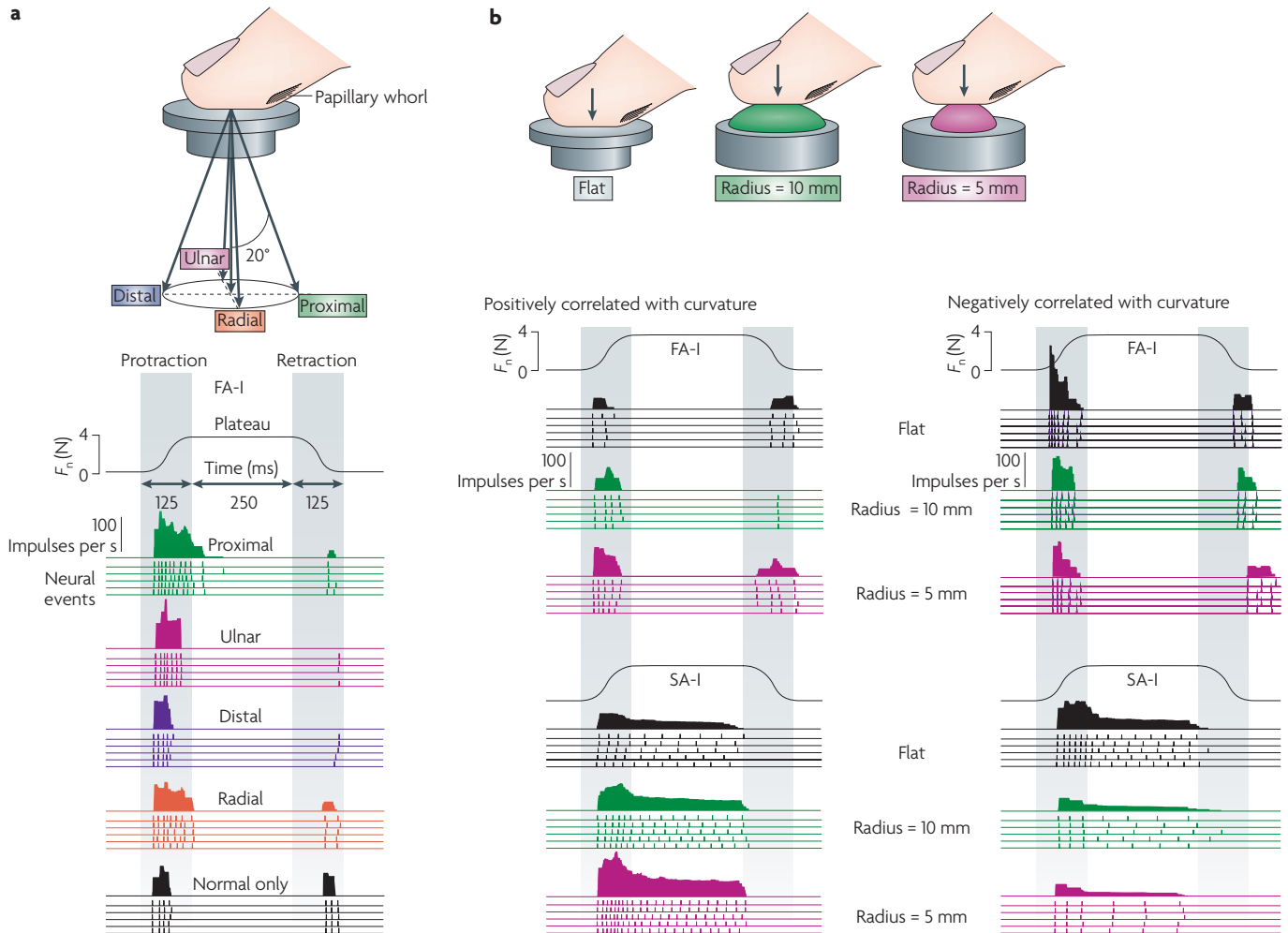
Occasionally, frictional slips occur that rapidly shift the object load from the slipping digit to the other

digits engaged in gripping the object. Such load shifts, which are reliably signalled by FA-I afferents<sup>2,96</sup>, trigger a phase-appropriate corrective action that results in a lasting update of grip-to-load force ratios at the engaged

### Box 3 | Sensorimotor control points in a prototypic object manipulation task

Manipulation tasks are characterized by a sequence of action phases separated by contact events that define task subgoals. Consider the task of grasping an object, lifting it from a table, holding it in the air and then replacing it (see part **a** of the figure)<sup>63</sup>. The goal of the initial reach phase is marked by the digits contacting the object and the goal of the subsequent load phase is marked by the breaking of contact between the object and the support surface. These and subsequent contact events correspond to discrete sensory events that are characterized by specific afferent neural signatures in the tactile modality (part **b**) and often in the auditory and visual modalities (not shown). Such signatures specify the functional goals of successive action phases. In addition to generating motor commands, each action-phase controller predicts the sensory events that signify subgoal attainment. Thus, the brain can monitor task progression and produce corrective actions if mismatches are detected. Recordings of tactile afferent signals in single neurons of the human median nerve during the lift and replace task<sup>11</sup> have shown that there are distinct discharges from the fingertips at four points corresponding to subgoal events (part **b**): responses primarily in FA-I (fast-adapting type I) afferents when the object is contacted and released and responses in FA-II afferents related to the transient mechanical events that accompany the object lifting off and being replaced on the support surface. In addition to responses to distinct contact events, many SA-I (slow-adapting type I) and SA-II afferents discharge when static forces are applied to the object. Figure is modified, with permission, from REF. 5 © (2008) Academic Press.





**Figure 1 | Encoding of fingertip force direction and contact surface shape.** **a** | Impulses in an FA-I (fast-adapting type I) afferent in response to repeated ( $n = 5$ ) application of force stimuli in different directions (colour coded in schematic and traces). The top trace for each direction shows the instantaneous discharge rate averaged over the five trials. The time course of force application, illustrated with the normal force component ( $F_n$ ), is also shown. The responsiveness of most FA-I, SA-I (slow-adapting type I) and SA-II afferents is broadly tuned to a preferred direction of force. For example, the afferent shown responded most intensely to tangential force increases in the proximal direction but also responded to tangential force increases in other directions. Across afferents, the preferred directions are distributed all around the angular space. **b** | Impulses in two FA-I and two SA-I afferents in response to repeated ( $n = 5$ ) stimuli with normal forces applied to a flat surface and two spherically curved surfaces. The left and right panels for each afferent type show example afferents with response intensities that increased and decreased, respectively, with the increase in curvature. Afferents with increased response intensity tend to terminate centrally in the contact area and those with decreased response intensity terminate at the sides and end of the fingertip. Part **a** is reproduced, with permission, from REF. 22 © (2001) Society for Neuroscience. Part **b** is modified, with permission, from REF. 23 © (2003) Blackwell Science.

digits<sup>63,73,91</sup> — for example, an increase in grip force during the hold phase or a slowing down of the load force rate during the load phase<sup>63</sup>.

Little is known about the central neural architecture that supports the control of grasp stability. For the basic grip force–load force coupling, brain imaging studies suggest that the right posterior parietal cortex<sup>104</sup> and the bilateral cerebellum<sup>105,106</sup> have important roles, at least in tasks performed with the right hand. Computational studies have referred to the cerebellum as a principal brain structure for the storage of forward internal models that support predictive motor control<sup>105,107</sup>. However,

patients with cerebellar lesions exhibit various impairments of grip force–load force coupling<sup>108–113</sup>, and so the role of the cerebellum is far from clear. Furthermore, basic grip force–load force coupling seems to be surprisingly robust to a variety of cerebral lesions<sup>114–116</sup>, and TMS-induced lesions of the primary sensorimotor cortex<sup>60</sup>, the premotor cortex<sup>62</sup> and the posterior parietal cortex<sup>61</sup> have shown only subtle effects on this coupling. Evidence from patients with abnormal corticospinal projections suggests that grip force–load force coupling that supports grasp stability can be implemented independent of signals in fast corticospinal pathways<sup>117</sup>.

**Forward internal models**  
Neural circuits that mimic the behaviour of the motor system and environment and capture the mapping between motor commands and expected sensory consequences.

Even less is known about the central neural mechanisms that support adaptation of grip-to-load force ratios to changes in an object's surface properties. TMS stimulation of the left anterior intraparietal area ~150 ms before grasp contact seems to disturb this adaptation in object lifting, resulting in inflated grip forces<sup>61</sup>. Likewise, TMS-induced temporary lesions targeting the primary motor cortex can also perturb the control of grip-to-load force ratios<sup>62,118,119</sup>. In addition, various central neural disruptions can result in elevated grip forces during object manipulation, including those that result from cerebral stroke<sup>114,115</sup>, amyotrophic lateral sclerosis<sup>120</sup>, cerebellar disease<sup>110–113</sup>, basal ganglia disease<sup>116,121–123</sup> and writer's cramp<sup>124,125</sup>. Accordingly, an increased grip-to-load force ratio may reflect a 'default' strategy used in various conditions to overcome the failure in effectively adapting the force coordination for grasp stability<sup>126</sup>.

#### *Contacts between objects in the hand and other objects.*

Ensembles of FA-II afferents that terminate throughout the hand signal the incidence and dynamic aspects of contact between hand-held objects and other objects<sup>11</sup>. Such events occur, for example, in tool use and in lifting tasks when the contact between a grasped object and the support surface breaks and when the object contacts the support when it is being replaced (BOX 3). When we lift an object, information about its weight cannot be obtained until the object breaks contact with the supporting surface. Therefore, efficient lifting involves making accurate predictions of the required load force. Such predictions may come from previous experience of lifting that particular object<sup>127</sup>, from learned size–weight associations for the kind of object being lifted<sup>128–132</sup> or from learned links between arbitrary visual or auditory cues and an object's weight<sup>133,134</sup>.

If these predictions are erroneous, corrective action programmes triggered by the mismatch between the predicted and the actual sensory events related to lift-off are launched automatically (FIG. 2a,b). In addition, the memory supporting the weight prediction for the object is updated. Often, a single lift can efficiently bring about such updating<sup>127,129</sup>, although repeated interactions with the object may be required for adequate updating under unusual conditions<sup>128–131,135,136</sup>.

Recent experiments using event-related functional MRI (fMRI) during lifting tasks involving the right hand suggest that the right inferior parietal cortex has an important role in detecting mismatches between predicted and actual weight<sup>137</sup> (FIG. 2c). The connectivity of this region, which receives inputs from sensory cortices and has reciprocal connections to various motor regions, seems to be suitable for detecting and classifying performance errors. Results from TMS studies suggest that the posterior parietal cortex is also crucial for dynamic error detection in visually guided reaching and reach-to-grasp actions<sup>138,139</sup>. fMRI results indicate that both the primary sensorimotor cortex and the cerebellum are engaged in implementing corrective action programmes triggered by poor weight prediction, but in a way that depends on the nature of the mismatch between the predicted and the actual weight<sup>137</sup>. When

the weight of an object is underestimated (FIG. 2b), the sensorimotor cortex shows greater activation during the increase in fingertip forces that occurs while probing for tactile events signalling lift-off than when the weight is accurately predicted (FIG. 2c). There is decreased activation in the cerebellum in such instances. The opposite pattern of activity occurs when the weight is overestimated (FIG. 2c). That is, there is increased activation in the cerebellum and decreased activation in the sensorimotor cortex. Thus, neural activity in the cerebellum seems to increase during the implementation of corrective actions only when information about the object's actual weight, obtained at lift-off (FIG. 2a), is already available (that is, when the object has been lifted but its weight is less than predicted). This observation agrees with results which suggest that the anterior cerebellar cortex is involved in recruiting internal representations of object properties<sup>140</sup> and also agrees with the general notion that transmitting sensorimotor knowledge from the cerebellum to the motor cortex allows efficient execution of learned motor responses<sup>141</sup>. TMS-induced lesions of the primary sensorimotor cortex contralateral to the lifting hand can disrupt weight prediction in object lifting based on somatosensory information acquired in a previous lift<sup>142</sup>. By contrast, such lesions do not disrupt predictions of object weight based on learned arbitrary colour cues, whereas TMS-induced lesions of the dorsal premotor area do<sup>142</sup>. Importantly, these results suggest that anticipatory parametric adaptation of action-phase controllers to object properties can rely on partly distinct neural networks, depending on the context in which the underlying representation was formed. With respect to predicting object weight on the basis of size, observations in a patient with a left temporoparietal lesion suggest that the left parietal cortex is required<sup>143</sup>. Taken together, these studies provide interesting examples of how the different brain areas that support control mechanisms in object manipulation can be teased apart.

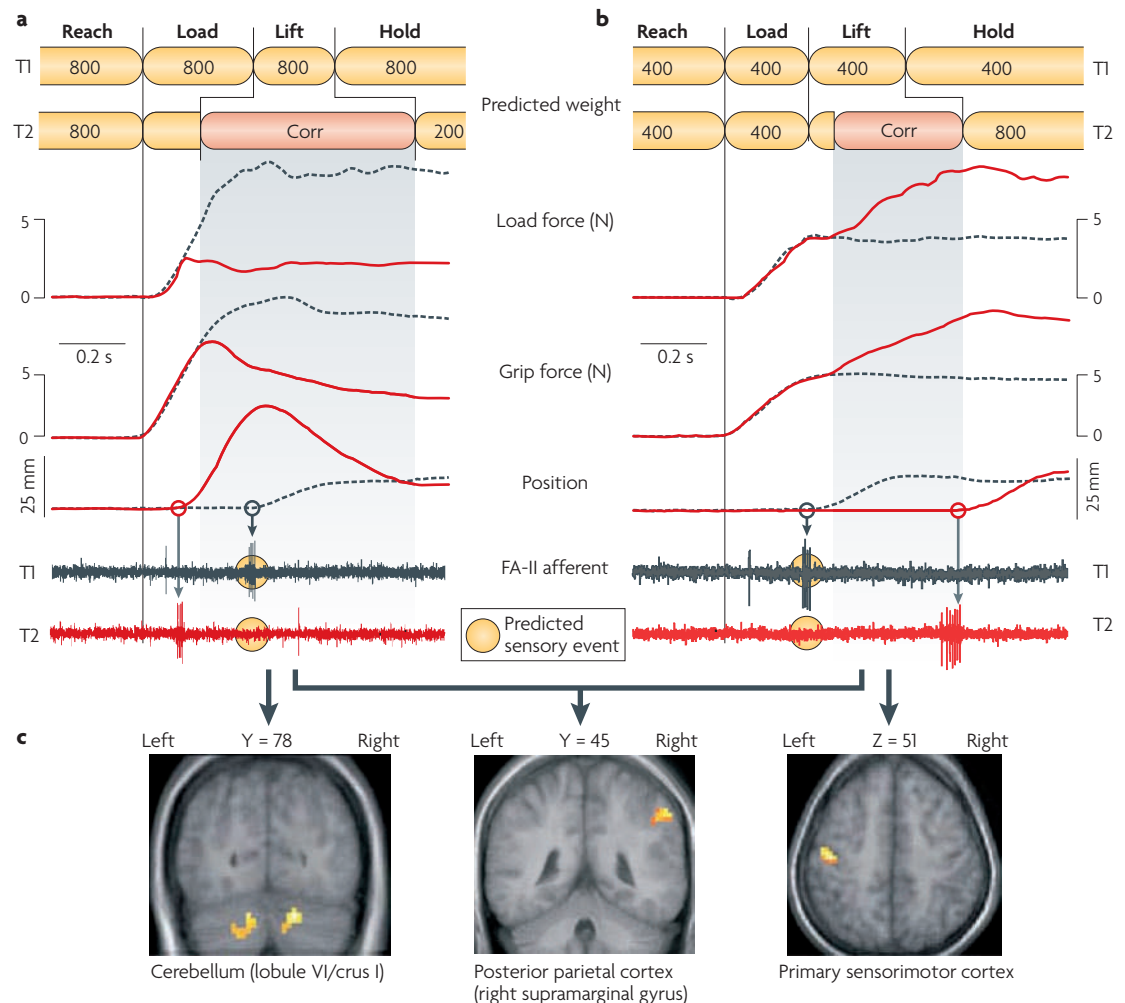
#### **Spike timing offers fast afferent information**

**Rate coding versus relative spike timing.** Following Adrian's discoveries in the 1920s<sup>144</sup>, most studies have assumed that tactile afferents convey information in their firing rates (rate coding)<sup>14–19,145</sup>. This requires a given neuron to fire at least two impulses. However, the speed with which the brain detects and classifies prediction errors in the tactile modality and launches corrective actions implies that some information can be transmitted even when most of the afferents recruited have only had time to fire one impulse<sup>146</sup>. This suggests that the relative timing of impulses in individual tactile afferents in ensembles conveys important information.

Recently, it has been demonstrated that the relative timing of the first spikes that are elicited in ensembles of tactile afferents when objects are contacted provides precise information about the shape of the contacted surface as well as the direction of the force exerted on the hand<sup>146</sup>, and that it does so fast enough to account for the speed with which tactile signals are used in object manipulation tasks. Changes in either surface shape or force direction can alter the first-spike latency

of individual afferents without significantly affecting the distribution of first-spike latencies in the afferent population as a whole. Changes in contact parameters can therefore reliably influence the sequence in which different members of afferent populations first respond to

tactile events. For a code based on relative spike timing to be effective, sufficient numbers of afferents must be recruited. This is ensured by the high density of afferents, especially in the fingertips<sup>103</sup> (TABLE 1), and by the large degree of functional overlap of receptive fields<sup>147</sup>.



**Figure 2 | Corrective actions triggered by a mismatch between predicted and actual sensory events.** The traces in parts **a** and **b** show load force, grip force, object position and afferent responses, as a function of time, as a subject grasps, lifts and holds aloft an object. **a** | Data for when a participant lifted an 800 g object (T1; grey dashed curves) expecting it to weigh 800 g and then lifted a 200 g object (T2; red curves) expecting it to also weigh 800 g. The top diagram represents the predictions that were fed to the action-phase controllers. When the load-phase controller is primed for a weight that is greater than the actual weight of the object (T2), FA-II (fast-adapting type II) afferents signal lift-off before the predicted time (circles behind the nerve traces). This unpredicted sensory event triggers abortion of the implemented controller and execution of a corrective action programme (corr) that brings the object back to the intended position. The lift movement becomes faster and higher than intended because the corrective action kicks in after a ~100 ms sensorimotor delay (see position signal, T2). **b** | The participant also lifted an 800 g object (T2; red curves) while expecting a 400 g weight lifted previously (T1; grey dashed curves). The load phase terminated before the lift-off and the subsequent lift-phase controller was implemented while the object was still standing on its support (T2). In this situation, the absence of an expected sensory event signalling lift-off at the predicted time triggers a corrective action consisting of slow, probing increases in fingertip forces that continue until they are terminated by sensory events signalling lift-off. **c** | Functional MRI recordings indicate that a mismatch between predicted and actual weight activates the right posterior parietal cortex regardless of whether the weight is lighter or heavier than predicted (middle panel). With the load-phase controller targeted for a heavier weight (as in part **a**), the corrective action correlates with increased neural activity in the cerebellum (left panel), whereas there is increased activity in the primary sensorimotor cortex if the controller is targeted for a lighter weight (right panel). Traces for load force, grip force and position in parts **a** and **b** are modified, with permission, from REF. 127 © (1988) Springer Verlag. Afferent recordings in part **a** are reproduced from REF. 233. Afferent recordings in part **b** are reproduced, with permission, from REF. 234 © (1992) Elsevier. Part **c** is modified, with permission, from REF. 137 © (2006) Society for Neuroscience.



Estimates indicate that the FA-I population can discriminate different surface curvatures and force directions after as few as five afferents have begun firing<sup>146</sup>. A correspondingly reliable discrimination by the SA-I population requires approximately twice as many afferents to fire because of a larger variability in first-spike latencies. Nevertheless, relative spike timing allows much more rapid discrimination than rate coding in ensembles of afferents, providing a time gain of at least 15–20 ms<sup>146</sup>. SA-II afferents are much less useful for the fast discrimination of force direction or object shape by either coding scheme, because these afferents have relatively poor dynamic sensitivity and many of them have relatively high background firing levels. The relative timing of impulses presumably also contains information about other crucial initial contact parameters, such as the frictional condition and contact events that occur between held objects and other objects.

Research on the central processing of various sensory modalities indicates that the precise timing of neural discharges can carry far more information than firing rates alone<sup>148,149</sup>. The significance of first spikes, in particular, has been emphasized for the auditory<sup>150,151</sup>, visual<sup>152–154</sup> and somatosensory<sup>155,156</sup> systems. However, the existence of effective codes based on spike timing does not exclude the possibility that average firing rates also carry information in neural networks<sup>157</sup>. The lack of a consistent relationship between the latencies for response onsets and firing rates in tactile afferents suggests that these two codes in fact provide independent information about tactile events<sup>146</sup>. It is possible that different codes are used by different processes and by the different pathways that use tactile afferent information. For example, relative spike timing may primarily support fast stimulus classification in the control of action, which operates on rapidly varying signals. Firing rates, by contrast, might preferentially support perceptual mechanisms that operate under less time pressure and, often, on steadier signals. Furthermore, the fact that the two codes seem to convey similar information but in apparently independent ways suggests that they represent complementary monitoring systems. This might be useful for learning, verifying and upholding the function of various control processes.

***A proposed model for the processing of tactile afferent information.*** If precise spike timing is fundamental to the rapid encoding and transfer of tactile information in object manipulation, a crucial issue is how such information can be decoded. We do not think that the brain can use decoding schemes that quantify spike latency information using an independent and precise internal time reference<sup>158</sup>, because it is unlikely that the brain can predict contact events with millisecond precision in manipulation tasks. Instead, we propose that the brain exploits one of its most fundamental computational mechanisms — namely coincidence detection, in which central neurons preferentially respond when receiving synchronous inputs from many sources<sup>159–161</sup>. Synchronous inputs at a neuron not only evoke larger postsynaptic potentials than asynchronous inputs, according to mechanisms of

spike timing-dependent synaptic plasticity they can also bring about learning<sup>162–168</sup>.

We argue that the design of the somatosensory pathways could enable rapid classification of tactile stimuli by temporal-to-spatial conversion at the level of second-order neurons (in the cuneate nucleus and spinal cord), which may function as coincidence detectors. First, the patterns of divergence and convergence of primary afferents onto second-order neurons would enable second-order neurons to uniquely encode a massive number of different first-spike timing patterns. A single primary afferent fibre from the skin may project to ~1,700 cuneate neurons<sup>169</sup>, and ~2,000 tactile afferents innervate each fingertip<sup>103</sup>; however, each cuneate neuron receives signals from ~300 cutaneous afferents<sup>169</sup>, and so ~11,000 second-order cuneate neurons could be engaged in classifying stimuli at each fingertip. Thus, for one contact-surface shape, highly synchronous heterosynaptic inputs will occur at one or more second-order neurons whereas, for a different contact-surface shape, synchronous inputs will occur at a different set of second-order neurons (FIG. 3).

Second, the variation in axonal conduction velocity between afferents of the same functional type<sup>20,170,171</sup> is a robust feature of the PNS that might enhance stimulus classification based on coincidence detectors. This variation implies that the relative timing of spikes elicited in ensembles of tactile afferents changes when the spikes propagate along the afferent axon from the fingertip to the synaptic terminals at the second-order neurons (FIG. 3). With a conduction distance of ~1 m, the dispersion of conduction velocities results in conduction times that range from ~14 to 28 ms among afferents<sup>20,170,171</sup>. This increases the distribution of spike timing (compared with the periphery) by ~14 ms at the level of the second-order neurons, and corresponds to an approximate doubling of the latency effects observed on individual afferents with changes in contact parameters<sup>146</sup>. Indeed, coincidence detectors combined with different transmission delays along separate converging neural pathways have previously been implicated as a mechanism that can convert information contained in the relative timing of individual spikes into a place code for further processing<sup>148,163,172</sup>. Simulation studies using realistic neuron models and afferent signal patterns are needed to obtain credible estimates of the capacity of the proposed model to classify tactile events in terms of their stimuli at the level of both second- and higher-order neurons.

### Multisensory representation of action goals

We have argued that the tactile system predicts and monitors the timing and the physical nature of the discrete mechanical events that represent the outcomes of action phases. Studies of gaze behaviour in object manipulation suggest that predicting and monitoring sensory states also involves the visual modality. When people direct actions towards visible objects, action-phase controllers provide instructions for task- and phase-specific eye movements so as to acquire visual information that supports the planning and control of hand actions<sup>173,174</sup>. At the start of most action phases congruent hand and

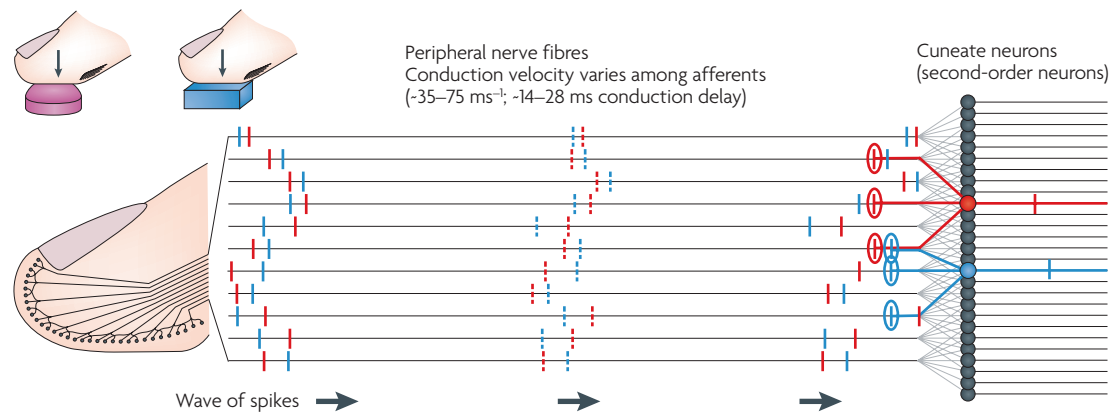


Figure 3 | **Hypothetical model for the fast processing of afferent information in somatosensory pathways.**

Second- (and higher-) order neurons function as coincidence detectors and so are sensitive to specific spatiotemporal properties of impulse patterns in a population of tactile afferents. The first waves of impulses in an ensemble of afferents in response to the fingertip contacting objects with two types of surface shape (flat and curved) are schematically illustrated. The stimulus shape influences the first-spike latencies of the responsive afferents. The substantial divergence and convergence of primary afferents onto second-order neurons and the dispersion of conduction velocities among afferents provide parallel processing of the temporally structured information that aids feed-forward rapid classification of information by temporal-to-spatial conversion.

eye movements to the contact location are launched concurrently, based on information from peripheral vision<sup>174–178</sup>. The high speed of eye movements implies that the gaze reaches the contact location well before the hand (FIG. 4a,b). Importantly, this gaze behaviour develops gradually during the learning of required action-phase controllers. That is, during learning the gaze behaviour gradually shifts from pursuing poorly controlled hand movements to a mode in which the gaze predicts forthcoming contact locations<sup>179</sup>, corroborating the notion that learning to predict sensory consequences of motor commands precedes accurate control<sup>81</sup>.

Early fixations of contact locations can support online movement adjustments based on sensed and/or predicted gaze-position signals<sup>180</sup> and on visual feedback of hand movements referenced to the foveated target<sup>176,181–183</sup>. However, the gaze often remains at the contact location, such that the final part of the action phase, during which visual information can no longer influence the hand movement, is captured in central vision (FIG. 4c). The fact that the gaze often shifts to the goal of the next action phase around the predicted time of goal completion suggests that the visual system can both predict and monitor contact events representing completion of task subgoals.

Although tactile feedback related to control points is essential for skilled object manipulation, contact events can also be predicted and monitored in the visual modality (when visible) as well as the auditory and, presumably, the proprioceptive modalities. Multimodal encoding of sensorimotor control points probably allows the sensorimotor system to monitor multiple aspects of task performance and, if errors are detected, respond to the pattern of errors observed in different modalities. Furthermore, because many contact events give rise to salient sensory signals from multiple modalities that are linked in time and space, they provide an opportunity

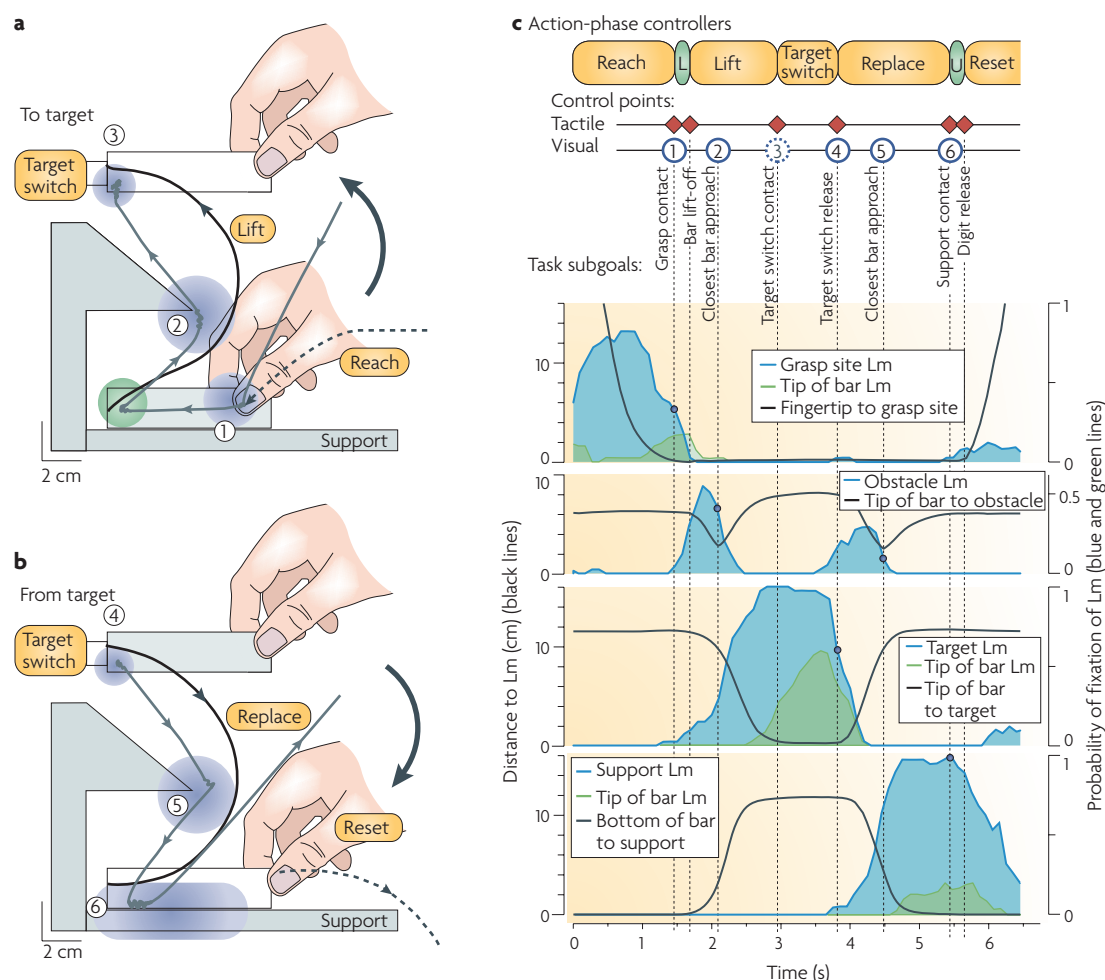
for sensorimotor integration and intermodal alignment, which are helpful for learning and upholding multimodal sensorimotor correlations that support the prediction of purposeful motor commands. It is indeed well established that the brain can automatically integrate temporally correlated information occurring in the somatosensory, auditory and visual modalities, and neural activity common to all three stimulus modalities is present in the parietal and frontal cortices<sup>184,185</sup> and in the posterior superior temporal sulcus<sup>186</sup>. Studies in such multisensory areas in monkeys indicate that the relative timing of convergent multimodal inputs is a crucial factor for neuronal responses<sup>187,188</sup>.

### Conclusions and future directions

Dexterous object manipulation serves as an interesting model system for sensorimotor control because it is explicitly concerned with interactions between the body and the environment, and because manipulation tasks are comprised of sequentially organized distinct movement phases. These features are key components of most natural actions, ranging from tool use to locomotion. We have proposed that crucial control operations are centred on events that mark transitions between consecutive action phases and that represent task subgoals. At these events, the brain both receives and makes predictions about sensory information from multiple sources. Thus, these events serve as control points that enable the upholding, adaptation and learning of sensorimotor correlations that are used to guide future action. In addition, they enable a comparison of context-specific predictions of the sensory outcome (corollary discharge) of planned actions and the actual sensory outcome. Through such comparisons, errors in prediction can be detected and used to launch corrective action patterns as required. In general terms, our framework agrees with control theories which imply that control turns desired sensory

#### Corollary discharge

An internal signal, derived in part from motor commands, that can be used to estimate the time-varying afferent input that corresponds to the predicted sensory consequences of the motor command.



**Figure 4 | Visual and tactile control points in a manipulation task. a,b** | Gaze and hand movements when a person grasps a bar, moves it around an obstacle to press a target switch (**a**) and then replaces it on the support surface (**b**). The dashed black lines represent the path of the tip of the index finger, the solid black lines indicate the path of the tip of the bar and the grey lines indicate the gaze position. The blue and green areas indicate 'landmark' (Lm) zones that captured 90% of the fixations recorded during several trials by ten participants. These zones are centred on the grasp site, the tip of the bar (green), the protruding part of the obstacle, the target and the support surface. **c** | Coordination of gaze and manual actions. The blue and green lines give the time-varying instantaneous probability of gaze fixations in the landmark zones listed, and the black lines indicate the distance between the landmark and either the tip of the index finger, the tip of the bar or the bottom of the bar (indicated for each graph). The red diamonds indicate tactile control points and the blue circles indicate contact events predicted in the visual modality. The spatial locations of these events are indicated by the location of the correspondingly numbered circle in parts **a** and **b**. This figure demonstrates that the gaze is directed to key locations that represent task subgoals. The fact that the gaze shifts to the goal of the next action phase around the predicted time of goal completion suggests that the visual system can both predict and monitor contact events representing subgoal completion. Figure is modified, with permission, from REF. 177 © (2001) Society for Neuroscience.

states into motor commands and prediction maps motor commands into expected sensory consequences<sup>189–191</sup>. Furthermore, the idea that control is centred on distinct movement goals is consistent with a recent computational model of sensorimotor control referred to as optimal feedback control<sup>192–194</sup>. Learned action-phase controllers correct errors only if they influence the movement goal, and each controller flexibly combines sensory signals and efferent copies of motor commands to optimize its performance.

However, defining the principles for the planning and control of actions based on behavioural observations does not provide direct knowledge of the neural mechanisms

involved. Although numerous studies have examined the central neural mechanisms that support the planning and control of reaching, much less is known about object manipulation (for a review see REF. 195). Over the past two decades, a number of studies have attempted to address this knowledge deficit. Although these studies have generated knowledge about the brain areas that are engaged during manipulation<sup>195</sup>, an understanding of how defined control operations that support natural manipulation tasks are implemented in the CNS is just beginning to emerge. There are many challenges involved in developing this understanding. For example, it might be difficult to define the embodiment of a given manipulation task

in the neural networks of the CNS, because the various action-phase controllers that are brought into play might all use different processes to some extent, in part depending on the nature of the sensory information involved. There is indeed evidence that elementary action phases can be organized in various areas of the CNS, from spinal cord networks to frontoparietal cortical networks<sup>196–198</sup>. Furthermore, a challenging issue is how to distinguish processes involved in detecting mismatches from those involved in triggering corrective actions and those involved in creating, containing and recruiting relevant internal representations during the progression of manipulation tasks. This requires analysis of the dynamics of the system. New analysis methods applicable to studies in humans might help, such as dynamic causal modelling<sup>199</sup>, which is used to infer processes and mechanisms at the neuronal level from measurements of brain activity obtained with different techniques.

In the field of motor control, most studies have focused on single actions, such as moving the hand between two points in space, and have therefore overlooked a crucial component of natural tasks: namely that they consist of a series of phases demarcated by discrete events that provide subgoals for task completion. Although there is evidence in monkeys that the prefrontal cortex plays a part in assembling sequences of action-phase controllers for completing manual tasks<sup>200–202</sup>, little is known about the mechanisms that are used to coordinate the sensory interactions and predictions across the action-phase controllers, as required for smooth linking of action phases. Given that the correct sequence of actions in everyday tasks normally has to be learned or selected through experience, understanding how movement phases are put together is also important for the study of motor learning. An important component of skill development probably involves combining previously learnt action-phase controllers in new ways. This ability requires learning to predict event-related sensory outcomes under new conditions. Similarly, little is known about how the lateralized brain flexibly and swiftly allocates complementary

roles to the hands during the sequential action phases that are involved in natural bimanual object manipulation tasks. Whereas research on bimanual coordination has focused on situations in which the two hands have difficulty acting independently<sup>203–205</sup>, recent work has started to examine the flexible coordination of the hands in skilled bimanual manipulation<sup>206,207</sup>.

Even at the level of the basic tactile afferent mechanisms there are numerous unresolved issues. One important problem for future research concerns how the brain deals with the complex interaction effects among the different parameters of fingertip stimulation, which affect the afferent responses that arise. For example, there are interactions between force direction and object shape that affect the firing rates<sup>23</sup> and relative spike timing<sup>146</sup> of the afferent responses. In addition, the recent stimulus history can also influence the afferent responses, because of the viscoelastic properties of the fingertips<sup>22,49,208</sup>. A more general issue concerns how the brain processes tactile afferent signals to detect spatiotemporal events that are conditional on, and specific for, the implemented action-phase controller and its current state. In this context, one may speculate that many of the computational requirements for decoding tactile messages are satisfied by the somatosensory pathways that functionally model the mechanical state of the fingertips by, in effect, filtering information predictively in a manner that is specific for the active action-phase controller and its current phase. Indeed, a large proportion of the descending information from sensorimotor cortical areas targets nodes of the somatosensory pathways through corticothalamic, corticocuneate and corticospinal pathways and could thus dynamically control signal processing in ascending somatosensory pathways<sup>209–214</sup>. Such mechanisms are in agreement with recent work that has identified a pivotal role for corollary discharges at different levels of the CNS in affecting the processing of sensory afferent information<sup>215,216</sup>, including at low levels of the sensory pathways such as the primary afferent axon terminal and/or first-order interneurons<sup>213,216</sup>.

- Macefield, V. G. & Johansson, R. S. Control of grip force during restraint of an object held between finger and thumb: responses of muscle and joint afferents from the digits. *Exp. Brain Res.* **108**, 172–184 (1996).
- Macefield, V. G., Häger-Ross, C. & Johansson, R. S. Control of grip force during restraint of an object held between finger and thumb: responses of cutaneous afferents from the digits. *Exp. Brain Res.* **108**, 155–171 (1996).
- Häger-Ross, C. & Johansson, R. S. Non-digital afferent input in reactive control of fingertip forces during precision grip. *Exp. Brain Res.* **110**, 131–141 (1996).
- Dimitriou, M. & Edin, B. B. Discharges in human muscle receptor afferents during block grasping. *J. Neurosci.* **28**, 12632–12642 (2008).
- Johansson, R. S. & Flanagan, J. R. in *The Senses: a Comprehensive Reference*, Volume 6, *Somatosensation* (eds Gardner, E. & Kaas, J. H.) 67–86 (Academic, San Diego, 2008).
- Vallbo, A. B. & Johansson, R. S. Properties of cutaneous mechanoreceptors in the human hand related to touch sensation. *Hum. Neurobiol.* **3**, 3–14 (1984).
- Johansson, R. S., Landström, U. & Lundström, R. Responses of mechanoreceptive afferent units in the glabrous skin of the human hand to sinusoidal skin displacements. *Brain Res.* **244**, 17–25 (1982).
- Löfvenberg, J. & Johansson, R. S. Regional differences and interindividual variability in sensitivity to vibration in the glabrous skin of the human hand. *Brain Res.* **301**, 65–72 (1984).
- Brisben, A. J., Hsiao, S. S. & Johnson, K. O. Detection of vibration transmitted through an object grasped in the hand. *J. Neurophysiol.* **81**, 1548–1558 (1999).
- Loewenstein, W. R. & Skalak, R. Mechanical transmission in a Pacinian corpuscle. An analysis and theory. *J. Physiol.* **182**, 346–378 (1966).
- Westling, G. & Johansson, R. S. Responses in glabrous skin mechanoreceptors during precision grip in humans. *Exp. Brain Res.* **66**, 128–140 (1987).
- Impulses in single tactile afferents innervating the human fingertips were recorded from the median nerve while small test objects were lifted, held in the air and then replaced. Distinct discharges were observed at various contact events corresponding to the completion of task subgoals.**
- Knibestöl, M. Stimulus-response functions of slowly adapting mechanoreceptors in the human glabrous skin area. *J. Physiol.* **245**, 63–80 (1975).
- Johansson, R. S. Tactile sensibility in the human hand: receptive field characteristics of mechanoreceptive units in the glabrous skin area. *J. Physiol.* **281**, 101–125 (1978).
- Darian-Smith, I. in *Handbook of Physiology* (eds, Brookhart, J. M., Mountcastle, V. B., Darian-Smith, I. & Geiger, S. R.) 739–788 (American Physiological Society, Bethesda, Maryland, 1984).
- Johnson, K. O., Yoshioka, T. & Vega-Bermudez, F. Tactile functions of mechanoreceptive afferents innervating the hand. *J. Clin. Neurophysiol.* **17**, 539–558 (2000).
- Goodwin, A. W. & Wheat, H. E. Sensory signals in neural populations underlying tactile perception and manipulation. *Annu. Rev. Neurosci.* **27**, 53–77 (2004).
- Johnson, K. O. & Hsiao, S. S. Neural mechanisms of tactual form and texture perception. *Annu. Rev. Neurosci.* **15**, 227–250 (1992).
- Craig, J. C. & Rollman, G. B. Somesthesia. *Annu. Rev. Psychol.* **50**, 305–331 (1999).
- Sathian, K., Goodwin, A. W., John, K. T. & Darian-Smith, I. Perceived roughness of a grating: correlation with responses of mechanoreceptive afferents innervating the monkey's fingerpad. *J. Neurosci.* **9**, 1273–1279 (1989).
- Johansson, R. S. & Vallbo, Å. B. Tactile sensory coding in the glabrous skin of the human hand. *Trends Neurosci.* **6**, 27–31 (1983).
- Bisley, J. W., Goodwin, A. W. & Wheat, H. E. Slowly adapting type I afferents from the sides and end of the finger respond to stimuli on the center of the fingerpad. *J. Neurophysiol.* **84**, 57–64 (2000).
- Birnie, L., Jenmalm, P., Goodwin, A. W. & Johansson, R. S. Encoding of direction of fingertip forces by human tactile afferents. *J. Neurosci.* **21**, 8222–8237 (2001).



23. Jenmalm, P., Birznieks, I., Goodwin, A. W. & Johansson, R. S. Influences of object shape on responses in human tactile afferents under conditions characteristic for manipulation. *Eur. J. Neurosci.* **18**, 164–176 (2003).
24. Hinton, G. E., McClelland, J. L. & Rumelhart, D. E. in *Parallel Distributed Processing* vol. 1 (eds Rumelhart, D. E. & McClelland, J. L.) 77–109 (MIT Press, Cambridge, Massachusetts, 1986).
25. Eurich, C. W. & Schwegler, H. Coarse coding: calculation of the resolution achieved by a population of large receptive field neurons. *Biol. Cybern.* **76**, 357–363 (1997).
26. Maeno, T. & Kobayashi, K. FE analysis of the dynamic characteristics of the human finger pad in contact with objects with/without surface roughness. *Proc. 1998 Am. Soc. Mech. Eng. Int. Mech. Eng. Congress Exposition* **64**, 279–286 (1998).
27. Maeno, T., Kobayashi, K. & Yamazaki, N. Relationship between the structure of human finger tissue and the location of tactile receptors. *JSMIE Int. J.* **41**, 94–100 (1998).
28. Serina, E. R., Mockensturm, E., Mote, C. D. Jr & Rempel, D. A structural model of the forced compression of the fingertip pulp. *J. Biomech.* **31**, 639–646 (1998).
29. Srinivasan, M. A. & Dandekar, K. An investigation of the mechanics of tactile sense using two-dimensional models of the primate fingertip. *J. Biomech. Eng.* **118**, 48–55 (1996).
30. Nakazawa, N., Ikeura, R. & Inooka, H. Characteristics of human fingertips in the shearing direction. *Biol. Cybern.* **82**, 207–214 (2000).
31. Dandekar, K., Raju, B. I. & Srinivasan, M. A. 3-D finite-element models of human and monkey fingertips to investigate the mechanics of tactile sense. *J. Biomech. Eng.* **125**, 682–691 (2003).
32. Wu, J. Z., Dong, R. G., Smutz, W. P. & Schopper, A. W. Modeling of time-dependent force response of fingertip to dynamic loading. *J. Biomech.* **36**, 383–392 (2003).
33. Wu, J. Z., Welcome, D. E. & Dong, R. G. Three-dimensional finite element simulations of the mechanical response of the fingertip to static and dynamic compressions. *Comput. Methods Biomech. Biomed. Eng.* **9**, 55–63 (2006).
34. Maeno, T., Kawamura, T. & Cheng, S. C. Friction estimation by pressing an elastic finger-shaped sensor against a surface. *IEEE Trans. Rob. Autom.* **20**, 222–228 (2004).
35. Flanagan, J. R., Bowman, M. C. & Johansson, R. S. Control strategies in object manipulation tasks. *Curr. Opin. Neurobiol.* **16**, 650–659 (2006).
36. Prochazka, A. The fuzzy logic of visuomotor control. *Can. J. Physiol. Pharmacol.* **74**, 456–462 (1996).
37. Misiaszek, J. E. Neural control of walking balance: if falling then react else continue. *Exerc. Sport Sci. Rev.* **34**, 128–134 (2006).
38. Forssberg, H., Eliasson, A. C., Kinoshita, H., Johansson, R. S. & Westling, G. Development of human precision grip. I: Basic coordination of force. *Exp. Brain Res.* **85**, 451–457 (1991).
39. Forssberg, H. et al. Development of human precision grip. II. Anticipatory control of isometric forces targeted for object's weight. *Exp. Brain Res.* **90**, 393–398 (1992).
40. Gordon, A. M., Forssberg, H., Johansson, R. S., Eliasson, A. C. & Westling, G. Development of human precision grip. III. Integration of visual size cues during the programming of isometric forces. *Exp. Brain Res.* **90**, 399–403 (1992).
41. Forssberg, H., Eliasson, A. C., Kinoshita, H., Westling, G. & Johansson, R. S. Development of human precision grip. IV. Tactile adaptation of isometric finger forces to the frictional condition. *Exp. Brain Res.* **104**, 323–330 (1995).
42. Eliasson, A. C. et al. Development of human precision grip. V. Anticipatory and triggered grip actions during sudden loading. *Exp. Brain Res.* **106**, 425–433 (1995).
43. Paré, M. & Dugas, C. Developmental changes in prehension during childhood. *Exp. Brain Res.* **125**, 239–247 (1999).
44. Goodale, M. A. et al. Separate neural pathways for the visual analysis of object shape in perception and prehension. *Curr. Biol.* **4**, 604–610 (1994).
45. Santello, M. & Soechting, J. F. Gradual molding of the hand to object contours. *J. Neurophysiol.* **79**, 1307–1320 (1998).
46. Cohen, R. G. & Rosenbaum, D. A. Where grasps are made reveals how grasps are planned: generation and recall of motor plans. *Exp. Brain Res.* **157**, 486–495 (2004).
47. Cuijpers, R. H., Smeets, J. B. & Brenner, E. On the relation between object shape and grasping kinematics. *J. Neurophysiol.* **91**, 2598–2606 (2004).
48. Lukos, J., Ansuini, C. & Santello, M. Choice of contact points during multidigit grasping: effect of predictability of object center of mass location. *J. Neurosci.* **27**, 3894–3903 (2007).
49. Pawluk, D. T. & Howe, R. D. Dynamic lumped element response of the human fingerpad. *J. Biomech. Eng.* **121**, 178–183 (1999).
50. Wheat, H. E., Goodwin, A. W. & Browning, A. S. Tactile resolution: peripheral neural mechanisms underlying the human capacity to determine positions of objects contacting the fingerpad. *J. Neurosci.* **15**, 5582–5595 (1995).
51. Knibestöl, M. Stimulus-response functions of rapidly adapting mechanoreceptors in human glabrous skin area. *J. Physiol.* **232**, 427–452 (1973).
52. Johansson, R. S. & Vallbo, Å. B. in *Sensory Functions of the Skin in Primates, With Special Reference to Man* (ed. Zotterman, Y.) 171–184 (Pergamon, Oxford, 1976).
53. Gentilucci, M., Toni, I., Daprati, E. & Gangitano, M. Tactile input of the hand and the control of reaching to grasp movements. *Exp. Brain Res.* **114**, 130–137 (1997).
54. Lackner, J. R. & DiZio, P. A. Aspects of body self-calibration. *Trends Cogn. Sci.* **4**, 279–288 (2000).
55. Rao, A. K. & Gordon, A. M. Contribution of tactile information to accuracy in pointing movements. *Exp. Brain Res.* **138**, 438–445 (2001).
56. Gordon, A. M. & Soechting, J. F. Use of tactile afferent information in sequential finger movements. *Exp. Brain Res.* **107**, 281–292 (1995).
57. Rabin, E. & Gordon, A. M. Tactile feedback contributes to consistency of finger movements during typing. *Exp. Brain Res.* **155**, 362–369 (2004).
58. Säfström, D. & Edin, B. B. Task requirements influence sensory integration during grasping in humans. *Learn. Mem.* **11**, 356–363 (2004).
59. Lemon, R. N., Johansson, R. S. & Westling, G. Corticospinal control during reach, grasp and precision lift in man. *J. Neurosci.* **15**, 6145–6156 (1995).
60. Schabrun, S. M., Ridding, M. C. & Miles, T. S. Role of the primary motor and sensory cortex in precision grasping: a transcranial magnetic stimulation study. *Eur. J. Neurosci.* **27**, 750–756 (2008).
61. Davare, M., Andres, M., Clerget, E., Thonnard, J. L. & Olivier, E. Temporal dissociation between hand shaping and grip force scaling in the anterior intraparietal area. *J. Neurosci.* **27**, 3974–3980 (2007).
62. Davare, M., Andres, M., Cosnard, G., Thonnard, J. L. & Olivier, E. Dissociating the role of ventral and dorsal premotor cortex in precision grasping. *J. Neurosci.* **26**, 2260–2268 (2006).
63. Johansson, R. S. & Westling, G. Roles of glabrous skin receptors and sensorimotor memory in automatic control of precision grip when lifting rougher or more slippery objects. *Exp. Brain Res.* **56**, 550–564 (1984). **This study demonstrated that subjects' grip forces change in parallel with load forces to overcome forces counteracting the intended manipulation, and that the balance between the grip and load forces is adapted to the friction to provide a small safety margin to prevent slips. Experiments with local anaesthesia showed that this adaptation depends on cutaneous afferent input.**
64. Goodwin, A. W., Jenmalm, P. & Johansson, R. S. Control of grip force when tilting objects: effect of curvature of grasped surfaces and of applied tangential torque. *J. Neurosci.* **18**, 10724–10734 (1998).
65. Wing, A. M. & Lederman, S. J. Anticipating load torques produced by voluntary movements. *J. Exp. Psychol. Hum. Percept. Perform.* **24**, 1571–1581 (1998).
66. Johansson, R. S., Backlin, J. L. & Burstedt, M. K. O. Control of grasp stability during pronation and supination movements. *Exp. Brain Res.* **128**, 20–30 (1999).
67. Flanagan, J. R. & Wing, A. M. The stability of precision grip forces during cyclic arm movements with a hand-held load. *Exp. Brain Res.* **105**, 455–464 (1995).
68. Flanagan, J. R. & Tresilian, J. R. Grip load force coupling: a general control strategy for transporting objects. *J. Exp. Psychol. Hum. Percept. Perform.* **20**, 944–957 (1994).
69. LaMotte, R. H. Softness discrimination with a tool. *J. Neurophysiol.* **83**, 1777–1786 (2000).
70. Flanagan, J. R., Burstedt, M. K. O. & Johansson, R. S. Control of fingertip forces in multi-digit manipulation. *J. Neurophysiol.* **81**, 1706–1717 (1999).
71. Santello, M. & Soechting, J. F. Force synergies for multifingered grasping. *Exp. Brain Res.* **133**, 457–467 (2000).
72. Johansson, R. S. & Westling, G. Programmed and triggered actions to rapid load changes during precision grip. *Exp. Brain Res.* **71**, 72–86 (1988).
73. Burstedt, M. K. O., Edin, B. B. & Johansson, R. S. Coordination of fingertip forces during human manipulation can emerge from independent neural networks controlling each engaged digit. *Exp. Brain Res.* **117**, 67–79 (1997).
74. Bracewell, R. M., Wing, A. M., Soper, H. M. & Clark, K. G. Predictive and reactive co-ordination of grip and load forces in bimanual lifting in man. *Eur. J. Neurosci.* **18**, 2396–2402 (2003).
75. Witney, A. G., Goodbody, S. J. & Wolpert, D. M. Predictive motor learning of temporal delays. *J. Neurophysiol.* **82**, 2039–2048 (1999).
76. Gysin, P., Kaminski, T. R. & Gordon, A. M. Coordination of fingertip forces in object transport during locomotion. *Exp. Brain Res.* **149**, 371–379 (2003).
77. Witney, A. G. & Wolpert, D. M. The effect of externally generated loading on predictive grip force modulation. *Neurosci. Lett.* **414**, 10–15 (2007).
78. Danion, F. & Sarlegna, F. R. Can the human brain predict the consequences of arm movement corrections when transporting an object? Hints from grip force adjustments. *J. Neurosci.* **27**, 12839–12843 (2007).
79. Bursztyn, L. L. & Flanagan, J. R. Sensorimotor memory of weight asymmetry in object manipulation. *Exp. Brain Res.* **184**, 127–133 (2008).
80. Flanagan, J. R. & Wing, A. M. The role of internal models in motion planning and control: evidence from grip force adjustments during movements of hand-held loads. *J. Neurosci.* **17**, 1519–1528 (1997). **This study showed that when moving hand-held objects, people precisely modulate their grip force in anticipation of movement-dependent loads. This result provides strong evidence that the brain learns and makes use of accurate internal models of object mechanics to predict the consequences of action.**
81. Flanagan, J. R., Vetter, P., Johansson, R. S. & Wolpert, D. M. Prediction precedes control in motor learning. *Curr. Biol.* **13**, 146–150 (2003).
82. Westling, G. & Johansson, R. S. Factors influencing the force control during precision grip. *Exp. Brain Res.* **53**, 277–284 (1984).
83. Jenmalm, P. & Johansson, R. S. Visual and somatosensory information about object shape control manipulative finger tip forces. *J. Neurosci.* **17**, 4486–4499 (1997). **This study showed that people can use vision to predictively adapt their fingertip forces to the angle of grasped surfaces. The results also showed that, in the absence of vision, tactile information obtained when the fingertips contact the grasped surfaces can be used to rapidly adjust fingertip forces.**
84. Jenmalm, P., Dahlstedt, S. & Johansson, R. S. Visual and tactile information about object curvature control fingertip forces and grasp kinematics in human dexterous manipulation. *J. Neurophysiol.* **84**, 2984–2997 (2000).
85. Monzée, J., Lamarre, Y. & Smith, A. M. The effects of digital anesthesia on force control using a precision grip. *J. Neurophysiol.* **89**, 672–683 (2003).
86. Nowak, D. A., Glasauer, S. & Hermsdörfer, J. How predictive is grip force control in the complete absence of somatosensory feedback? *Brain* **127**, 182–192 (2004).
87. Nowak, D. A. & Hermsdörfer, J. Digit cooling influences grasp efficiency during manipulative tasks. *Eur. J. Appl. Physiol.* **89**, 127–133 (2003).
88. Cole, K. J., Steyers, C. M. & Graybill, E. K. The effects of graded compression of the median nerve in the carpal canal on grip force. *Exp. Brain Res.* **148**, 150–157 (2003).
89. Schenker, M., Burstedt, M. K., Wiberg, M. & Johansson, R. S. Precision grip function after hand replantation and digital nerve injury. *J. Plast. Reconstr. Aesthet. Surg.* **59**, 706–716 (2006).
90. Cadoret, G. & Smith, A. M. Friction, not texture, dictates grip forces used during object manipulation. *J. Neurophysiol.* **75**, 1963–1969 (1996).
91. Edin, B. B., Westling, G. & Johansson, R. S. Independent control of fingertip forces at individual digits during precision lifting in humans. *J. Physiol.* **450**, 547–564 (1992).
92. Birznieks, I., Burstedt, M. K. O., Edin, B. B. & Johansson, R. S. Mechanisms for force adjustments to unpredictable frictional changes at individual digits during two-fingered manipulation. *J. Neurophysiol.* **80**, 1989–2002 (1998).

93. Burstedt, M. K. O., Flanagan, R. & Johansson, R. S. Control of grasp stability in humans under different frictional conditions during multi-digit manipulation. *J. Neurophysiol.* **82**, 2393–2405 (1999).
94. Quaney, B. M. & Cole, K. J. Distributing vertical forces between the digits during gripping and lifting: the effects of rotating the hand versus rotating the object. *Exp. Brain Res.* **155**, 145–155 (2004).
95. Niu, X., Latash, M. L. & Zatsiorsky, V. M. Prehension synergies in the grasps with complex friction patterns: local versus synergic effects and the template control. *J. Neurophysiol.* **98**, 16–28 (2007).
96. Johansson, R. S. & Westling, G. Signals in tactile afferents from the fingers eliciting adaptive motor responses during precision grip. *Exp. Brain Res.* **66**, 141–154 (1987).
97. Sathian, K. Tactile sensing of surface features. *Trends Neurosci.* **12**, 513–519 (1989).
98. Johansson, R. S., Landström, U. & Lundström, R. Sensitivity to edges of mechanoreceptive afferent units innervating the glabrous skin of the human hand. *Brain Res.* **244**, 27–35 (1982).
99. Phillips, J. R., Johansson, R. S. & Johnson, K. O. Representation of braille characters in human nerve fibres. *Exp. Brain Res.* **81**, 589–592 (1990).
100. Phillips, J. R., Johansson, R. S. & Johnson, K. O. Responses of human mechanoreceptive afferents to embossed dot arrays scanned across fingerpad skin. *J. Neurosci.* **12**, 827–839 (1992).
101. Goodwin, A. W., Macefield, V. G. & Bissley, J. W. Encoding of object curvature by tactile afferents from human fingers. *J. Neurophysiol.* **78**, 2881–2888 (1997).
102. Khalsa, P. S., Friedman, R. M., Srinivasan, M. A. & Lamotte, R. H. Encoding of shape and orientation of objects indented into the monkey fingerpad by populations of slowly and rapidly adapting mechanoreceptors. *J. Neurophysiol.* **79**, 3238–3251 (1998).
103. Johansson, R. S. & Vallbo, A. B. Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J. Physiol.* **286**, 283–300 (1979).
104. Ehrsson, H. E., Fagergren, A., Johansson, R. S. & Forssberg, H. Evidence for the involvement of the posterior parietal cortex in coordination of fingertip forces for grasp stability in manipulation. *J. Neurophysiol.* **90**, 3295–3303 (2003).
105. Kawato, M. *et al.* Internal forward models in the cerebellum: fMRI study on grip force and load force coupling. *Prog. Brain Res.* **142**, 171–188 (2003).
106. Boecker, H. *et al.* Force level independent representations of predictive grip force-load force coupling: a PET activation study. *Neuroimage* **25**, 243–252 (2005).
107. Wolpert, D. M., Miall, C. R. & Kawato, M. Internal models in the cerebellum. *Trends Cogn. Sci.* **2**, 338–347 (1998).
108. Rost, K., Nowak, D. A., Timmann, D. & Hermsdörfer, J. Preserved and impaired aspects of predictive grip force control in cerebellar patients. *Clin. Neurophysiol.* **116**, 1405–1414 (2005).
109. Nowak, D. A., Hermsdörfer, J., Marquardt, C. & Fuchs, H. H. Grip and load force coupling during discrete vertical arm movements with a grasped object in cerebellar atrophy. *Exp. Brain Res.* **145**, 28–39 (2002).
110. Müller, F. & Dichgans, J. Dyscoordination of pinch and lift forces during grasp in patients with cerebellar lesions. *Exp. Brain Res.* **101**, 485–492 (1994).
111. Babin-Ratté, S., Sirigu, A., Gilles, M. & Wing, A. Impaired anticipatory finger grip-force adjustments in a case of cerebellar degeneration. *Exp. Brain Res.* **128**, 81–85 (1999).
112. Serrien, D. J. & Wiesendanger, M. Role of the cerebellum in tuning anticipatory and reactive grip force responses. *J. Cogn. Neurosci.* **11**, 672–681 (1999).
113. Fellows, S. J., Ernst, J., Schwarz, M., Töpper, R. & Noth, J. Precision grip deficits in cerebellar disorders in man. *Neurophysiol. Clin.* **112**, 1793–1802 (2001).
114. Hermsdörfer, J., Hagl, E., Nowak, D. A. & Marquardt, C. Grip force control during object manipulation in cerebral stroke. *Clin. Neurophysiol.* **114**, 915–929 (2003).
115. Nowak, D. A., Hermsdörfer, J. & Topka, H. Deficits of predictive grip force control during object manipulation in acute stroke. *J. Neurol.* **250**, 850–860 (2003).
116. Müller, F. & Abbs, J. H. in *Advances in Neurology* vol. 53 (eds Streifler, M. B., Korezyn, A. D., Melamed, E. & Youdim, M. B. H.) 191–195 (Raven, New York, 1990).
117. Harrison, L. M., Mayston, M. J. & Johansson, R. S. Reactive control of precision grip does not depend on fast transcortical reflex pathways in X-linked Kallmann subjects. *J. Physiol.* **527**, 641–652 (2000).
118. Nowak, D. A., Voss, M., Huang, Y. Z., Wolpert, D. M. & Rothwell, J. C. High-frequency repetitive transcranial magnetic stimulation over the hand area of the primary motor cortex disturbs predictive grip force scaling. *Eur. J. Neurosci.* **22**, 2392–2396 (2005).
119. Berner, J., Schönfeldt-Lecuona, C. & Nowak, D. A. Sensorimotor memory for fingertip forces during object lifting: the role of the primary motor cortex. *Neuropsychologia* **45**, 1931–1938 (2007).
120. Nowak, D. A., Hermsdörfer, J. & Topka, H. When motor execution is selectively impaired: control of manipulative finger forces in amyotrophic lateral sclerosis. *Motor Control* **7**, 304–320 (2003).
121. Gordon, A. M., Quinn, L., Reilmann, R. & Marder, K. Coordination of prehensile forces during precision grip in Huntington's disease. *Exp. Neurol.* **163**, 136–148 (2000).
122. Serrien, D. J., Burgunder, J. M. & Wiesendanger, M. Grip force scaling and sequencing of events during a manipulative task in Huntington's disease. *Neuropsychologia* **39**, 734–741 (2001).
123. Fellows, S. J., Noth, J. & Schwarz, M. Precision grip and Parkinson's disease. *Brain* **121**, 1771–1784 (1998).
124. Serrien, D. J., Burgunder, J. M. & Wiesendanger, M. Disturbed sensorimotor processing during control of precision grip in patients with writer's cramp. *Mov. Disord.* **15**, 965–972 (2000).
125. Schenk, T. & Mai, N. Is writer's cramp caused by a deficit of sensorimotor integration? *Exp. Brain Res.* **136**, 321–330 (2001).
126. Wiesendanger, M. & Serrien, D. J. Neurological problems affecting hand dexterity. *Brain Res. Brain Res. Rev.* **36**, 161–168 (2001).
127. 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).
128. Gordon, A. M., Forssberg, H., Johansson, R. S. & Westling, G. Integration of sensory information during the programming of precision grip: comments on the contributions of size cues. *Exp. Brain Res.* **85**, 226–229 (1991).
129. Gordon, A. M., Westling, G., Cole, K. J. & Johansson, R. S. Memory representations underlying motor commands used during manipulation of common and novel objects. *J. Neurophysiol.* **69**, 1789–1796 (1993).
- The authors showed that humans use anticipatory control to scale motor commands to the weight of familiar objects. The memory information is robust and can be retrieved through visual identification of the target object. In addition, accurate memory representations related to the weights of novel objects develop quickly.**
130. Flanagan, J. R. & Beltzner, M. A. Independence of perceptual and sensorimotor predictions in the size-weight illusion. *Nature Neurosci.* **3**, 737–741 (2000).
131. Flanagan, J. R., Bittner, J. P. & Johansson, R. S. Experience can change distinct size-weight priors engaged in lifting objects and judging their weights. *Curr. Biol.* **18**, 1742–1747 (2008).
- This paper showed that the motor and perceptual systems rely on distinct learned size-weight maps when lifting objects and judging their weights, respectively, and that these maps can be changed by experience.**
132. Cole, K. J. Lifting a familiar object: visual size analysis, not memory for object weight, scales lift force. *Exp. Brain Res.* **188**, 551–557 (2008).
133. Cole, K. J. & Rotella, D. L. Old age impairs the use of arbitrary visual cues for predictive control of fingertip forces during grasp. *Exp. Brain Res.* **143**, 35–41 (2002).
134. Ameli, M., Dafotakis, M., Fink, G. R. & Nowak, D. A. Predictive force programming in the grip-lift task: the role of memory links between arbitrary cues and object weight. *Neuropsychologia* **46**, 2383–2388 (2008).
135. Salimi, I., Hollender, I., Frazier, W. & Gordon, A. M. Specificity of internal representations underlying grasping. *J. Neurophysiol.* **84**, 2390–2397 (2000).
136. Salimi, I., Frazier, W., Reilmann, R. & Gordon, A. M. Selective use of visual information signaling objects' center of mass for anticipatory control of manipulative fingertip forces. *Exp. Brain Res.* **150**, 9–18 (2003).
137. Jenmalm, P., Schmitz, C., Forssberg, H. & Ehrsson, H. H. Lighter or heavier than predicted: neural correlates of corrective mechanisms during erroneously programmed lifts. *J. Neurosci.* **26**, 9015–9021 (2006).
- This study examined central contributions to precision lifting using fMRI. The results suggested a role for the right inferior parietal cortex in detecting mismatches between predicted and actual weight and indicated that the primary sensorimotor cortex and the cerebellum are engaged in implementing corrective action programmes.**
138. Desmurget, M. *et al.* Role of the posterior parietal cortex in updating reaching movements to a visual target. *Nature Neurosci.* **2**, 563–567 (1999).
139. Tunik, E., Frey, S. H. & Grafton, S. T. Virtual lesions of the anterior intraparietal area disrupt goal-dependent on-line adjustments of grasp. *Nature Neurosci.* **8**, 505–511 (2005).
140. Bursztyn, L. L., Ganesh, G., Imamura, H., Kawato, M. & Flanagan, J. R. Neural correlates of internal-model loading. *Curr. Biol.* **16**, 2440–2445 (2006).
141. Hua, S. E. & Houk, J. C. Cerebellar guidance of premotor network development and sensorimotor learning. *Learn. Mem.* **4**, 63–76 (1997).
142. Chouinard, P. A., Leonard, G. & Paus, T. Role of the primary motor and dorsal premotor cortices in the anticipation of forces during object lifting. *J. Neurosci.* **25**, 2277–2284 (2005).
- This paper showed that repetitive TMS applied to the dorsal premotor cortex disrupts associative memory for weight whereas repetitive TMS applied to the primary motor cortex disrupts sensorimotor memory for weight.**
143. Li, Y., Randerath, J., Goldenberg, G. & Hermsdörfer, J. Grip forces isolated from knowledge about object properties following a left parietal lesion. *Neurosci. Lett.* **426**, 187–191 (2007).
144. Adrian, E. D. *The Basis of Sensation* (Norton, New York, 1928).
145. Törebjörk, H. E., Vallbo, A. B. & Ochoa, J. L. Intraneural microstimulation in man. Its relation to specificity of tactile sensations. *Brain* **110**, 1509–1529 (1987).
146. Johansson, R. S. & Birznieks, I. First spikes in ensembles of human tactile afferents code complex spatial fingertip events. *Nature Neurosci.* **7**, 170–177 (2004).
- This study demonstrated that the relative timing of first impulses elicited in ensembles of tactile afferents when fingertips contact objects conveys information about the direction of fingertip forces and surface shape faster than the fastest possible rate code and fast enough to account for the use of this information in natural manipulations.**
147. Johansson, R. S. & Vallbo, A. B. Spatial properties of the population of mechanoreceptive units in the glabrous skin of the human hand. *Brain Res.* **184**, 353–366 (1980).
148. Heil, P. First-spike latency of auditory neurons revisited. *Curr. Opin. Neurobiol.* **14**, 461–467 (2004).
149. VanRullen, R., Guyonneau, R. & Thorpe, S. J. Spike times make sense. *Trends Neurosci.* **28**, 1–4 (2005).
150. Furukawa, S., Xu, L. & Middlebrooks, J. C. Coding of sound-source location by ensembles of cortical neurons. *J. Neurosci.* **20**, 1216–1228 (2000).
151. Nelken, I., Chechik, G., Mscis-Flogel, T. D., King, A. J. & Schnupp, J. W. Encoding stimulus information by spike numbers and mean response time in primary auditory cortex. *J. Comput. Neurosci.* **19**, 199–221 (2005).
152. Reich, D. S., Mechler, F. & Victor, J. D. Temporal coding of contrast in primary visual cortex: when, what, and why. *J. Neurophysiol.* **85**, 1039–1050 (2001).
153. Gawne, T. J., Kjaer, T. W. & Richmond, B. J. Latency: another potential code for feature binding in striate cortex. *J. Neurophysiol.* **76**, 1356–1360 (1996).
154. Golisch, T. & Meister, M. Rapid neural coding in the retina with relative spike latencies. *Science* **319**, 1108–1111 (2008).
- The authors reported that retinal ganglion cells can encode the spatial structure of a briefly presented image in the relative timing of their first spikes. This mechanism allows the retina to rapidly and reliably transmit new spatial information with the very first spikes emitted by a neural population in a manner that is largely unaffected by stimulus contrast.**
155. Panzeri, S., Petersen, R. S., Schultz, S. R., Lebedev, M. & Diamond, M. E. The role of spike timing in the coding of stimulus location in rat somatosensory cortex. *Neuron* **29**, 769–777 (2001).
156. Petersen, R. S., Panzeri, S. & Diamond, M. E. Population coding in somatosensory cortex. *Curr. Opin. Neurobiol.* **12**, 441–447 (2002).
157. Mikula, S. & Niebur, E. Rate and synchrony in feedforward networks of coincidence detectors: analytical solution. *Neural Comput.* **17**, 881–902 (2005).



158. Gerstner, W. & Kistler, W. M. *Spiking Neuron Models* (Cambridge Univ. Press, Cambridge, 2002).
159. Hopfield, J. J. Pattern recognition computation using action potential timing for stimulus representation. *Nature* **376**, 33–36 (1995).
160. König, P., Engel, A. K. & Singer, W. Integrator or coincidence detector? The role of the cortical neuron revisited. *Trends Neurosci.* **19**, 130–137 (1996).
161. Masquelier, T., Guyonnet, R. & Thorpe, S. J. Spike timing dependent plasticity finds the start of repeating patterns in continuous spike trains. *PLoS ONE* **3**, e1377 (2008).
162. Markram, H., Lübke, J., Frotscher, M. & Sakmann, B. Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. *Science* **275**, 213–215 (1997).
163. Bi, G. & Poo, M. Distributed synaptic modification in neural networks induced by patterned stimulation. *Nature* **401**, 792–796 (1999).
164. Song, S., Miller, K. D. & Abbott, L. F. Competitive Hebbian learning through spike-timing-dependent synaptic plasticity. *Nature Neurosci.* **3**, 919–926 (2000).
165. Fox, K. & Wong, R. O. A comparison of experience-dependent plasticity in the visual and somatosensory systems. *Neuron* **48**, 465–477 (2005).
166. Guyonnet, R., VanRullen, R. & Thorpe, S. J. Neurons tune to the earliest spikes through STDP. *Neural Comput.* **17**, 859–879 (2005).
167. Güttig, R. & Sompolinsky, H. The templotron: a neuron that learns spike timing-based decisions. *Nature Neurosci.* **9**, 420–428 (2006).
168. Chase, S. M. & Young, E. D. First-spike latency information in single neurons increases when referenced to population onset. *Proc. Natl Acad. Sci. USA* **104**, 5175–5180 (2007).
169. Jones, E. G. Cortical and subcortical contributions to activity-dependent plasticity in primate somatosensory cortex. *Annu. Rev. Neurosci.* **23**, 1–37 (2000).
170. Kakuda, N. Conduction velocity of low-threshold mechanoreceptive afferent fibers in the glabrous and hairy skin of human hands measured with microneurography and spike-triggered averaging. *Neurosci. Res.* **15**, 179–188 (1992).
171. Darian-Smith, I. & Kenins, P. Innervation density of mechanoreceptive fibres supplying glabrous skin of the monkey's index finger. *J. Physiol.* **309**, 147–155 (1980).
172. Carr, C. E. Processing of temporal information in the brain. *Annu. Rev. Neurosci.* **16**, 223–243 (1993).
173. Land, M. F. & Furneaux, S. The knowledge base of the oculomotor system. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **352**, 1231–1239 (1997).
174. Flanagan, J. R. & Johansson, R. S. Action plans used in action observation. *Nature* **424**, 769–771 (2003).
175. Ballard, D. H., Hayhoe, M. M., Li, F. & Whitehead, S. D. Hand-eye coordination during sequential tasks. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **337**, 331–338 (1992).
176. Land, M., Mennie, N. & Rusted, J. The roles of vision and eye movements in the control of activities of daily living. *Perception* **28**, 1311–1328 (1999).
177. Johansson, R. S., Westling, G., Bäckström, A. & Flanagan, J. R. Eye-hand coordination in object manipulation. *J. Neurosci.* **21**, 6917–6932 (2001). **This study examined the precise spatial and temporal coordination of gaze and fingertip movements in an object manipulation task. The results showed that the gaze supports hand movement planning by marking key positions to which the fingertips or the grasped object are subsequently directed.**
178. Biguer, B., Jeannerod, M. & Prablanc, C. The coordination of eye, head, and arm movements during reaching at a single visual target. *Exp. Brain Res.* **46**, 301–304 (1982).
179. Sailer, U., Flanagan, J. R. & Johansson, R. S. Eye–hand coordination during learning of a novel visuomotor task. *J. Neurosci.* **25**, 8833–8842 (2005). **This study examined changes in gaze behaviour during a visuomotor task in which subjects gradually learned a novel mapping between their hand actions and the movements of a cursor that they were required to move to targets. During learning, gaze behaviour shifted from a reactive mode, in which the gaze chased the cursor, to a predictive mode in which the gaze led the cursor to the targets.**
180. Prablanc, C., Desmurget, M. & Gréa, H. Neural control of on-line guidance of hand reaching movements. *Prog. Brain Res.* **142**, 155–170 (2003).
181. Paillard, J. Fast and slow feedback loops for the visual correction of spatial errors in a pointing task: a reappraisal. *Can. J. Physiol. Pharmacol.* **74**, 401–417 (1996).
182. Saunders, J. A. & Knill, D. C. Visual feedback control of hand movements. *J. Neurosci.* **24**, 3223–3234 (2004).
183. Sarlegna, F. *et al.* Online control of the direction of rapid reaching movements. *Exp. Brain Res.* **157**, 468–471 (2004).
184. Downar, J., Crawley, A. P., Mikulis, D. J. & Davis, K. D. A multimodal cortical network for the detection of changes in the sensory environment. *Nature Neurosci.* **3**, 277–283 (2000).
185. Bremner, F. *et al.* Polymodal motion processing in posterior parietal and premotor cortex: a human fMRI study strongly implies equivalencies between humans and monkeys. *Neuron* **29**, 287–296 (2001).
186. Beauchamp, M. S., Yasar, N. E., Frye, R. E. & Ro, T. Touch, sound and vision in human superior temporal sulcus. *Neuroimage* **41**, 1011–1020 (2008).
187. Avillac, M., Ben Hamed, S. & Duhamel, J. R. Multisensory integration in the ventral intraparietal area of the macaque monkey. *J. Neurosci.* **27**, 1922–1932 (2007).
188. Schroeder, C. E. & Foxe, J. J. The timing and laminar profile of converging inputs to multisensory areas of the macaque neocortex. *Brain Res. Cogn. Brain Res.* **14**, 187–198 (2002).
189. Miall, R. C. & Wolpert, D. M. Forward models for physiological motor control. *Neural Netw.* **9**, 1265–1279 (1996).
190. Wolpert, D. M. & Ghahramani, Z. Computational principles of movement neuroscience. *Nature Neurosci.* **3** (Suppl.), 1212–1217 (2000).
191. Wolpert, D. M. & Flanagan, J. R. Motor prediction. *Curr. Biol.* **11**, R729–R732 (2001).
192. Todorov, E. & Jordan, M. I. Optimal feedback control as a theory of motor coordination. *Nature Neurosci.* **5**, 1226–1235 (2002).
193. Scott, S. H. Optimal feedback control and the neural basis of volitional motor control. *Nature Rev. Neurosci.* **5**, 532–546 (2004).
194. Liu, D. & Todorov, E. Evidence for the flexible sensorimotor strategies predicted by optimal feedback control. *J. Neurosci.* **27**, 9354–9368 (2007).
195. Olivier, E., Davare, M., Andres, M. & Fadiga, L. Precision grasping in humans: from motor control to cognition. *Curr. Opin. Neurobiol.* **17**, 644–648 (2007).
196. Mussa-Ivaldi, F. A. & Bizzi, E. Motor learning through the combination of primitives. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **355**, 1755–1769 (2000).
197. Graziano, M. S. & Afalo, T. N. Mapping behavioral repertoire onto the cortex. *Neuron* **56**, 239–251 (2007).
198. Flash, T. & Hochner, B. Motor primitives in vertebrates and invertebrates. *Curr. Opin. Neurobiol.* **15**, 660–666 (2005).
199. Stephan, K. E. *et al.* Nonlinear dynamic causal models for fMRI. *Neuroimage* **42**, 649–662 (2008).
200. Averbeck, B. B., Chafee, M. V., Crowe, D. A. & Georgopoulos, A. P. Parallel processing of serial movements in prefrontal cortex. *Proc. Natl Acad. Sci. USA* **99**, 13172–13177 (2002).
201. Saito, N., Mushiaki, H., Sakamoto, K., Itoyama, Y. & Tanji, J. Representation of immediate and final behavioural goals in the monkey prefrontal cortex during an instructed delay period. *Cereb. Cortex* **15**, 1535–1546 (2005).
202. Tanji, J. & Hoshi, E. Role of the lateral prefrontal cortex in executive behavioral control. *Physiol. Rev.* **88**, 37–57 (2008).
203. Obhi, S. S. Bimanual coordination: an unbalanced field of research. *Motor Control* **8**, 111–120 (2004).
204. Swinnen, S. P. & Wenderoth, N. Two hands, one brain: cognitive neuroscience of bimanual skill. *Trends Cogn. Sci.* **8**, 18–25 (2004).
205. Ivry, R. B., Dierkerichsen, J., Spencer, R. C. M., Hazeltine, E. & Semjen, A. In *Neuro-behavioral Determinants of Interlimb Coordination* (eds Swinnen, S. & Duysens, J.) 259–295 (Kluwer, Boston, 2004).
206. Johansson, R. S. *et al.* How a lateralized brain supports symmetrical bimanual tasks. *PLoS Biol.* **4**, 1025–1034 (2006).
207. Theorin, A. & Johansson, R. S. Zones of bimanual and unimanual preference within human primary sensorimotor cortex during object manipulation. *Neuroimage* **36** (Suppl. 2), T2–T15 (2007).
208. Pubols, B. H. Jr. Factors affecting cutaneous mechanoreceptor response. II. Changes in mechanical properties of skin with repeated stimulation. *J. Neurophysiol.* **47**, 530–542 (1982).
209. Harris, F., Jabbur, S. J., Morse, R. W. & Towe, A. L. Influence of the cerebral cortex on the cuneate nucleus of the monkey. *Nature* **208**, 1215–1216 (1965).
210. Adkins, R. J., Morse, R. W. & Towe, A. L. Control of somatosensory input by cerebral cortex. *Science* **153**, 1020–1022 (1966).
211. Ergenzinger, E. R., Glasier, M. M., Hahn, J. O. & Pons, T. P. Cortically induced thalamic plasticity in the primate somatosensory system. *Nature Neurosci.* **1**, 226–229 (1998).
212. Palmeri, A., Bellomo, M., Giuffrida, R. & Sapienza, S. Motor cortex modulation of exteroceptive information at bulbar and thalamic lemniscal relays in the cat. *Neuroscience* **88**, 135–150 (1999).
213. Seki, K., Perlmutter, S. I. & Fetz, E. E. Sensory input to primate spinal cord is presynaptically inhibited during voluntary movement. *Nature Neurosci.* **6**, 1309–1316 (2003). **The authors reported evidence from behaving monkeys that presynaptic inhibition produced by central commands in descending pathways during wrist movements effectively modulates cutaneous inputs to the spinal cord in a behaviour-dependent manner by reducing synaptic transmission at the initial synapse.**
214. Canedo, A. Primary motor cortex influences on the descending and ascending systems. *Prog. Neurobiol.* **51**, 287–335 (1997).
215. Crapse, T. B. & Sommer, M. A. Corollary discharge circuits in the primate brain. *Curr. Opin. Neurobiol.* **1** Nov 2008 (doi:10.1016/j.conb.2008.09.017).
216. Poulet, J. F. & Hedwig, B. New insights into corollary discharges mediated by identified neural pathways. *Trends Neurosci.* **30**, 14–21 (2007).
217. von Holst, E. Relations between the central nervous system and the peripheral organ. *Br. J. Anim. Behav.* **2**, 89–94 (1954).
218. Boyd, I. A. & Roberts, T. D. Proprioceptive discharges from stretch-receptors in the knee-joint of the cat. *J. Physiol.* **122**, 38–58 (1953).
219. Gelfand, S. & Carter, S. Muscle sense in man. *Exp. Neurol.* **18**, 469–473 (1967).
220. Goodwin, G. M., McCloskey, D. I. & Matthews, P. B. The contribution of muscle afferents to kinaesthesia shown by vibration induced illusions of movement and by the effects of paralysing joint afferents. *Brain* **95**, 705–748 (1972).
221. Matthews, P. B. C. Where does Sherrington's "muscular sense" originate? Muscles, joints, corollary discharges? *Annu. Rev. Neurosci.* **5**, 189–218 (1982).
222. Johansson, R. S., Trulsson, M., Olsson, K. A. & Abbs, J. H. Mechanoreceptive afferent activity in the infraorbital nerve in man during speech and chewing movements. *Exp. Brain Res.* **72**, 209–214 (1988).
223. Edin, B. B. & Abbs, J. H. Finger movement responses of cutaneous mechanoreceptors in the dorsal skin of the human hand. *J. Neurophysiol.* **65**, 657–670 (1991).
224. Edin, B. B. Quantitative analysis of static strain sensitivity in human mechanoreceptors from hairy skin. *J. Neurophysiol.* **67**, 1105–1113 (1992).
225. Grill, S. E. & Hallett, M. Velocity sensitivity of human muscle spindle afferents and slowly adapting type II cutaneous mechanoreceptors. *J. Physiol.* **489**, 593–602 (1995).
226. Edin, B. B. Quantitative analyses of dynamic strain sensitivity in human skin mechanoreceptors. *J. Neurophysiol.* **92**, 3233–3243 (2004).
227. Edin, B. Cutaneous afferents provide information about knee joint movements in humans. *J. Physiol.* **531**, 289–297 (2001).
228. Aimonetti, J. M., Hospod, V., Roll, J. P. & Ribot-Ciscar, E. Cutaneous afferents provide a neuronal population vector that encodes the orientation of human ankle movements. *J. Physiol.* **580**, 649–658 (2007).
229. Edin, B. B. & Johansson, N. Skin strain patterns provide kinaesthetic information to the human central nervous system. *J. Physiol.* **487**, 243–251 (1995).
230. Collins, D. F. & Prochazka, A. Movement illusions evoked by ensemble cutaneous input from the dorsum of the human hand. *J. Physiol.* **496**, 857–871 (1996).
231. Collins, D. F., Refshauge, K. M. & Gandevia, S. C. Sensory integration in the perception of movements at the human metacarpophalangeal joint. *J. Physiol.* **529**, 505–515 (2000).
232. Collins, D. F., Refshauge, K. M., Todd, G. & Gandevia, S. C. Cutaneous receptors contribute to kinesthesia at the index finger, elbow, and knee. *J. Neurophysiol.* **94**, 1699–1706 (2005).
233. Johansson, R. S. & Edin, B. B. Predictive feed-forward sensory control during grasping and manipulation in man. *Biomed. Res.* **14**, 95–106 (1993).
234. Johansson, R. S. & Cole, K. J. Sensory-motor coordination during grasping and manipulative actions. *Curr. Opin. Neurobiol.* **2**, 815–823 (1992).

# Acknowledgements

The Swedish Research Council (project 08667), the sixth Framework Program of the EU (project IST-028056), and the Canadian Institutes of Health Research supported this work.