

WORKING MEMORY IN PRIMATE SENSORY SYSTEMS

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Abstract | Sensory working memory consists of the short-term storage of sensory stimuli to guide behaviour. There is increasing evidence that elemental sensory dimensions — such as object motion in the visual system or the frequency of a sound in the auditory system — are stored by segregated feature-selective systems that include not only the prefrontal and parietal cortex, but also areas of sensory cortex that carry out relatively early stages of processing. These circuits seem to have a dual function: precise sensory encoding and short-term storage of this information. New results provide insights into how activity in these circuits represents the remembered sensory stimuli.

Perception and memory are often depicted as separate processes, and researchers have often characterized the brain circuits that underlie perception and memory as distinct (and often anatomically distant) from each other. This review focuses on the neurocognitive mechanisms of working memory in primate sensory systems — the brief storage of sensory information that is used to guide our ongoing actions¹ — and its relationship to the mechanisms that underlie the processing of this information. We concentrate on studies that require subjects to hold information temporarily in short-term storage to perform a discrimination on a trial-by-trial basis. Various approaches have been used to investigate sensory working memory, ranging from psychophysics and functional imaging to single-cell recordings, electrical brain stimulation and studies of monkeys and humans with lesions. Psychophysical studies have focused on the properties of stimulus representations that are retained in working memory, whereas neurophysiological, imaging and lesion studies have focused on the regions in sensory cortex that analyse various stimulus features as well as focusing on the representation of sensory stimuli in regions that are traditionally associated with working memory, such as the prefrontal cortex (PFC) (BOX 1). The evidence that has emerged from these studies supports the idea that, in the primate brain, elemental sensory dimensions are represented by segregated memory systems that probably involve those cortical areas that are involved in encoding stimulus features, as well as prefrontal and parietal

regions. This circuitry supports the brief retention of sensory information for use in sensory-guided behaviour. Although much of the information about sensory working memory comes from studies of the visual system, there is a growing body of literature that deals with the storage of information in other sensory modalities, particularly tactile and auditory. The goal of this review is to discuss the key evidence that sensory cortical areas are an active component of the circuitry that underlies short-term retention of sensory signals. To facilitate comparison with work in non-human primates, this review is restricted to studies that used non-linguistic stimuli.

Visual working memory

Psychophysics. Visual working memory has been studied in subjects who performed tasks that involved delayed discrimination of basic stimulus attributes (such as size, orientation, contrast or direction of motion; FIG. 1a,b). The use of such stimuli offers the opportunity to test the ability to store parametric values of individual stimulus dimensions², and provides a quantitative measure of sensory storage by determining the threshold values that are needed for reliable retention of a sensory stimulus. Because the neuronal mechanisms that are involved in the encoding of many of these attributes have been extensively studied³, we can specify the effects of such stimuli on the initial stages of visual processing and can better understand the mechanisms that underlie their subsequent storage.

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Box 1 | Sensory signals in the prefrontal cortex

The prefrontal cortex (PFC) consists of several cytoarchitecturally defined regions. There is anatomical and physiological evidence that the PFC is functionally segregated with respect to sensory modalities and stimulus features^{85–87}. The physiological evidence includes reports that neurons in regions of the PFC that receive inputs from sensory neurons processing a particular stimulus feature respond selectively to that feature^{88–90}. On the other hand, there is accumulating evidence that many PFC neurons integrate information across sensory modalities^{91,92} and across different stimulus attributes within the same modality⁹³. One way to reconcile the apparent anatomical and functional segregation within the PFC with the presence of neurons that integrate information between different modalities and different stimulus features is to engage intrinsic connectivity within the PFC⁹⁴.

It is widely accepted that the PFC has a key role in sensory working memory. Although the mechanisms that underlie sensory storage are not well understood, most models of working memory (BOX 2) include cortical areas that process sensory information in the underlying circuitry^{95,96}. Indeed, many neurons in the PFC respond to the sensory stimuli that are used in working memory tasks^{93,88,97}. Furthermore, during a memory delay after a sensory cue, many PFC neurons show elevated cue-related activity that reflects the attributes of the relevant sensory modality^{88,97–101}. This activity has been interpreted as a mnemonic code that is used to retain sensory information (see, for example, REF. 102).

There is ample evidence for feedforward and feedback connections within sensory cortical areas and between those areas and the PFC¹⁰³. Although the precise nature of the interactions between neuronal populations in the PFC and sensory cortex during working memory tasks is not well understood, there is evidence for a dynamic interplay between them. The prevailing view, which is supported by studies of inferotemporal (IT) cortex in the absence of inputs from the PFC, is that the PFC exerts 'top-down' influences on sensory cortex^{44,104–106}. Additional support for top-down control comes from the observation that target selectivity seems to occur more rapidly in the PFC⁹⁹ than in IT cortex^{31,107}.

Many studies have shown that fundamental stimulus features such as orientation, size, speed or direction of motion can be retained in memory for many seconds, with little loss of information (FIG. 1b). There is also evidence that these distinct stimulus dimensions are stored by separate, feature-selective mechanisms⁴. For example, different features can be retained in working memory for different lengths of time (FIG. 1b): spatial frequency (size)^{5–8}, orientation^{9,10} or speed of motion can be retained for several seconds with little loss of precision, whereas the retention of luminance contrast^{11,12}, texture¹³, small spatial offsets (vernier stimuli)¹⁴ and direction of motion¹⁵ seem to be less robust. This apparently selective decay of information could indicate that there are separate storage processes for different stimulus features¹⁶. However, because the procedures that are used to study the retention of various stimulus attributes were not matched, some of the differences in decay functions could partly be due to procedural differences.

More compelling evidence in support of feature-selective retention mechanisms comes from studies that used interference consisting of an irrelevant stimulus, or 'memory mask', that is introduced during the memory delay (FIG. 2a). If such stimuli interfere with the memory representation, they produce a decrease in performance on the task. By manipulating the properties of the mask it is possible to gain insights into the nature of the remembered stimulus. For example, the ability of a masking grating to interfere with the delayed discrimination of spatial frequencies is greatest when the spatial

frequency of the mask differs from that of the remembered stimulus by at least an octave⁵. The effect is specific to the spatial frequency of the remembered grating and is unaffected by changes in the orientation of the mask. This selective interference indicates that information about spatial frequency is preserved by specialized mechanisms that are closely associated with those involved in its encoding, and are distinct from mechanisms that are concerned with stimulus orientation.

To investigate the dynamics of the storage process, another study used a spatial frequency discrimination task and introduced an interfering stimulus at different points during a 10-s delay¹⁷. The interfering stimulus was most effective when it was presented early in the delay, indicating that visual working memory might be a two-stage process: an initial short-lived perceptual encoding stage that is vulnerable to masking, and a more robust later stage. Memory tasks that involve visual motion are also more vulnerable to interference early in the delay period¹⁸.

Information about the speed and direction of visual motion can also be accurately preserved, sometimes for many seconds^{6,19}. To examine the nature of the retained speed information, an intervening mask, also consisting of a moving stimulus, was used while subjects compared two stimuli that moved at different speeds. The mask reduced the accuracy of performance only if its speed did not match the speed of the remembered stimulus, irrespective of its direction of motion. The selectivity of the masking effect, which resembled that of masking effects in memory for spatial frequency⁵, indicates that speed is faithfully preserved in memory and that the mechanisms of this preservation are relatively narrowly tuned. It also shows that speed and direction might be stored by separate mechanisms.

Selective retention of information about motion direction has been shown in monkeys that were required to compare two random-dot moving stimuli separated by a delay^{15,20,21}. The monkeys remembered the direction of coherent motion with only a modest decrease over time and reliably retained the direction of motion of stimuli with relatively low levels of coherence for as long as 4–6 s (REF. 15). In a subsequent study, the two comparison stimuli were spatially separated and a random-motion mask was introduced during the delay in either the sample location or the location of the upcoming test¹⁸ (FIG. 2a–c). The effect of the mask was specific to its properties and location (FIG. 2d,e). This selective interference indicates that the sensory attributes of visual motion are precisely preserved, which supports the idea that mechanisms that are involved in the processing of visual motion are also involved in its storage. Furthermore, this selectivity of masking effects resembles the selectivity that was seen in studies of memory for spatial frequency and speed^{5,6}, indicating that these different memory networks might share a similar architecture.

Evidence that the storage of visual motion in these tasks is specific for the location of the stimulus comes from a study²¹ that investigated the effect of spatial separation between the sample and test stimuli. The authors found that if the two comparison stimuli were

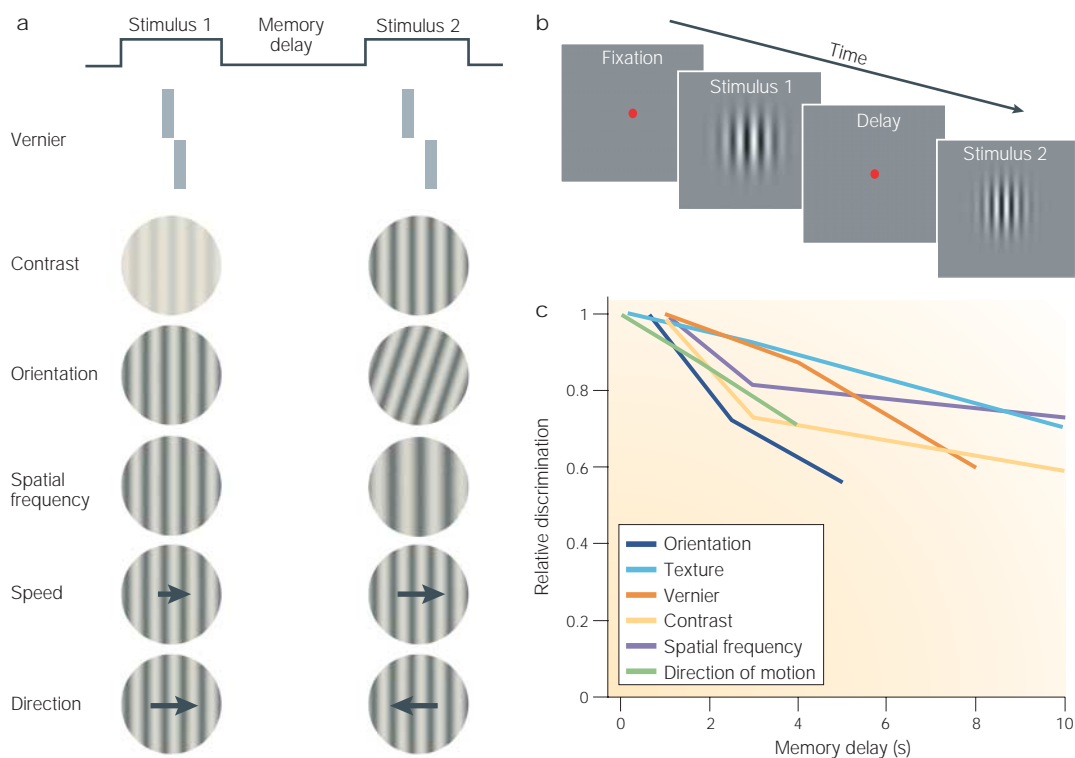


Figure 1 | Visual working memory for selected stimulus attributes. **a** | Delayed discrimination task and examples of visual stimuli that are commonly used to study the retention of stimulus attributes. Sinusoidal gratings are used to determine thresholds for discriminating contrast, orientation or other grating attributes. These thresholds (not shown) provide a measure of how well a given attribute is retained in memory. **b** | Typical behavioural paradigm. The trial begins with the onset of a central fixation point followed by a brief (200–500 ms) presentation of stimulus 1 (the ‘sample’ or ‘cue’). During the delay, the fixation target is present to aid fixation. At the end of the delay, the subject views stimulus 2 (the ‘test’), which differs from stimulus 1 along the dimension of interest (spatial frequency; for instance, bar width). The subject reports whether the second stimulus matches the first with respect to a given stimulus attribute. In the example shown, stimulus 2 has a higher spatial frequency than stimulus 1. **c** | Normalized discrimination sensitivity for various visual attributes plotted as a function of delay. The different curves were re-plotted from studies in which memory performance was evaluated for texture¹³, contrast⁷, vernier¹⁴, motion direction¹⁵, spatial frequency⁷ and orientation¹⁰. Although the retention of stimulus attributes degrades with time, this degradation is modest. Even after a 10-s delay, representation of some stimulus dimensions is degraded by no more than 25%.

spatially separated by more than a ‘critical’ separation, the threshold for discrimination of motion was elevated. They used the size of this separation to estimate the spatial extent of the mechanisms that were involved in the performance of the task. The critical separation increased with retinal eccentricity, and its size coincided with the size of receptive fields in cortical area MT, an area that is strongly associated with processing of visual motion, indicating that MT might be involved in performing the task. This finding supports the idea that retinotopically organized visual areas are involved in the storage of motion information.

Sekuler and colleagues used a different approach to examine the nature of stimulus representation in memory^{22,23}. In their task, subjects were presented with two consecutive texture stimuli followed by a probe stimulus, each consisting of vertical and horizontal sinusoidal gratings of varying spatial frequencies. The subjects had to judge only the vertical component of these textures and report whether the probe stimulus contained the same spatial frequency as either of the two preceding stimuli. The results supported the idea that the remembered spatial frequency of each stimulus evaluated during

the trial has a separate representation in memory that approximates the original stimulus but that is subject to noise and therefore constitutes a ‘noisy exemplar’.

Although the mechanisms that underlie the processing of colour have been extensively studied²⁴, relatively little is known about working memory for colour. Subjects retain information about hue with great precision²⁵, indicating that regions of the brain that are concerned with sensory processing of colour are also involved in this form of working memory. There is also evidence that the colour of an object can be processed separately from its location. In one study, colour or location distractors were introduced during the delay between two stimuli that differed in either colour or location²⁶. Location distractors interfered only with memory for location and not colour, whereas colour distractors interfered only with memory for colour, supporting the idea that memory for colour and spatial location are handled by separate systems. This conclusion is consistent with the notion that colour and location are processed by separate cortical visual pathways — the VENTRAL AND DORSAL STREAMS²⁷ — and indicates that this separation also holds for the temporary storage of these signals.

VENTRAL AND DORSAL VISUAL STREAMS

Visual information coming from V1 is processed in two interconnected but partly dissociable visual pathways, a ‘ventral’ pathway extending into the temporal lobe, which is thought to be primarily involved in visual object recognition, and a ‘dorsal’ pathway extending into the parietal lobes, which are thought to be more involved in extracting information about ‘where’ an object is or ‘how’ to execute visually guided action towards it.

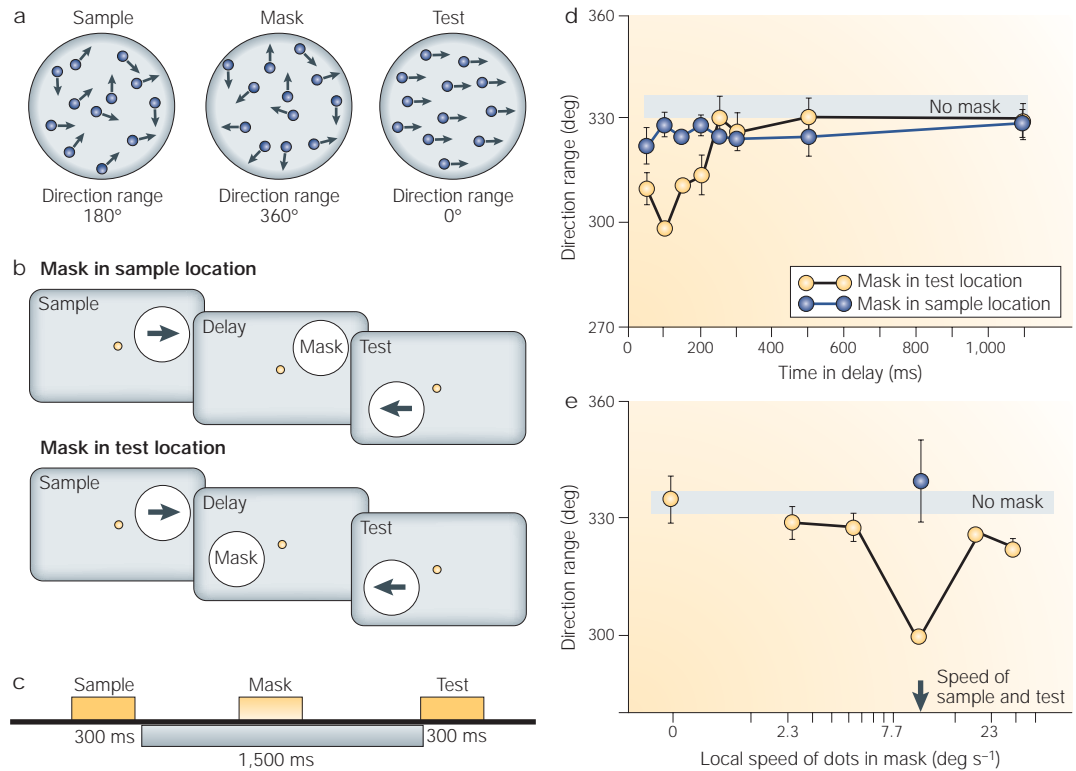


Figure 2 | Visual working memory for stimulus direction. **a** | Stimuli used to measure retention of motion direction in monkeys. **b** | Behavioural task. On each trial, the monkeys compared two directions of motion, sample and test, which were separated by a delay and in space. The sample consisted of random dots that moved in a variable range of directions; in the test stimulus, all the dots moved in the same direction. The monkeys reported whether the sample and test had the same mean direction of movement. The mask, consisting of dots moving in random directions (360° range), was introduced during the delay at the location of the preceding sample (upper row) or the upcoming test (lower row). **c** | Temporal parameters of the task. **d** | Temporal and spatial specificity of the remembered stimulus. Direction range thresholds are plotted as a function of the mask onset and location. Blue circles indicate thresholds measured with the mask at the sample location; yellow circles indicate thresholds measured with the mask at the test location. Grey bar, threshold value (\pm SEM) without the mask. The mask interfered with performance only when presented early in the delay at the location of the upcoming test. This indicates that the representation of remembered direction is spatially localized, is transferred to the site of the anticipated test, and is most vulnerable early in the delay. Deg, degrees. **e** | Stimulus specificity of the remembered sample. The local speeds of dots in the mask were varied. The mask decreased performance only when its local speeds matched the speed of the remembered sample, even though the monkey was not instructed to remember stimulus speed. This demonstrates that information about speed is preserved along with information about stimulus direction. Modified, with permission, from REF. 18 © (2002) Elsevier Science.

Overall, the mechanisms that preserve basic attributes of visual stimuli can be characterized as narrowly tuned, spatially localized filters, thereby supporting a model of working memory that involves the contribution of sensory cortical areas.

Physiology. Only a handful of neurophysiological studies have directly investigated the involvement of visual cortical areas in working memory. Until recently, much of the neurophysiological work on visual working memory has focused on the inferotemporal (IT) cortex, a relatively advanced stage of the ventral visual stream that is important for processing complex shapes²⁷. This work has shown that IT neurons in monkeys that have been trained to remember objects are active during the delay period after they have been shown the object, and that this activity is related to the remembered colour or shape^{28–31}. Memory-related activity elicited by both colour and motion has also been recorded in area V4, an earlier component of the ventral visual stream^{32,33}.

Recordings from regions in the parietal cortex that represent more advanced stages of processing in the dorsal visual stream also showed memory-related activity. For example, neurons in area 7a and the lateral intraparietal cortex (area LIP) fire while monkeys remember spatial locations³⁴. Ferrera *et al.*³² also found memory-related modulation of activity in area 7a while monkeys retained information about motion direction. These effects were largely absent in area MT, an earlier component of the dorsal pathway that is specialized for processing visual motion.

However, a recent study provided evidence for memory-related activity in area MT³⁵. In that study, the activity of MT neurons was recorded during a 1.5-s delay in a motion discrimination task (FIG. 3a). A typical neuron (FIG. 3a) was active not only in response to the sample and test stimuli, but also during the delay, when it showed a characteristic pattern of activity that consisted of a small burst of firing early in the delay, subsequent suppression of firing and then reactivation just before the presentation

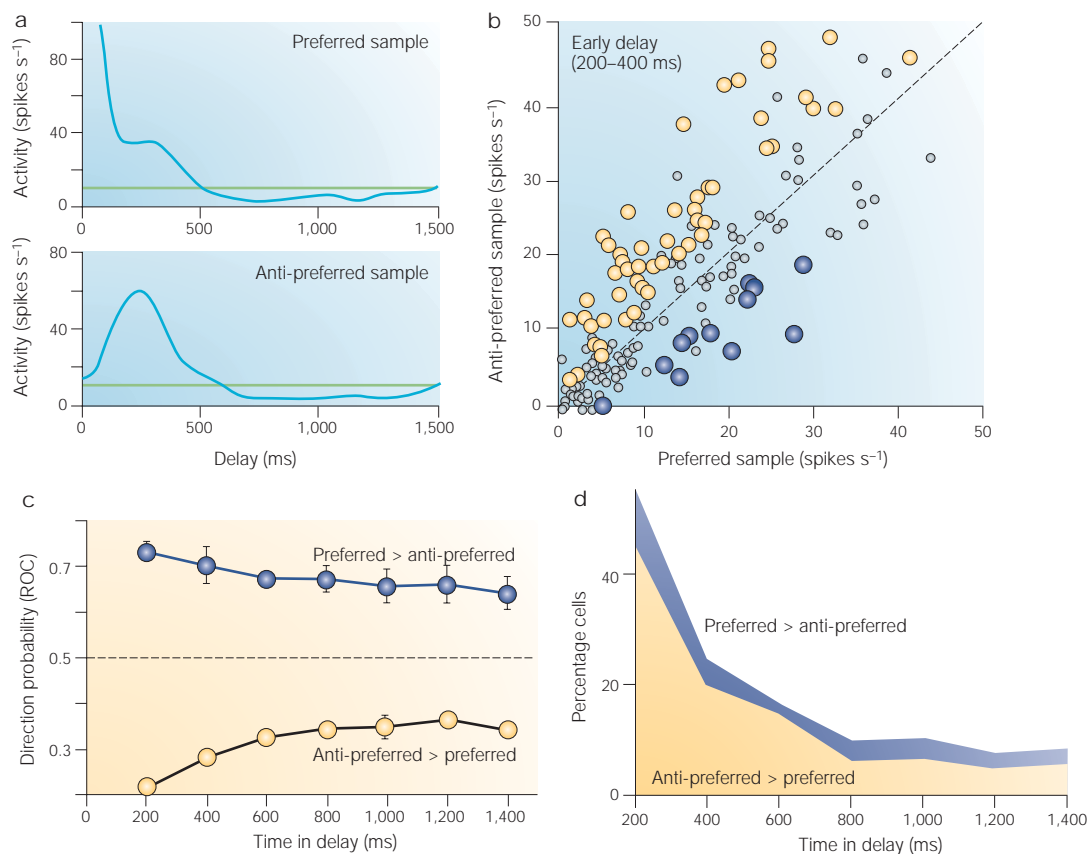


Figure 3 | Directional signals in area MT during the memory delay. **a** | Delay activity of an MT neuron during the working memory for motion task. Average firing rates recorded during the delay in a single testing session are shown as spike density functions for trials with sample moving in the preferred (top plot) and anti-preferred direction (bottom plot). Baseline activity (horizontal line) was recorded during fixation. This neuron shows a typical pattern of delay activity: brief early activation, prolonged suppression followed by a gradual increase in firing in anticipation of the end of the delay. **b** | Firing rates of individual neurons during early delay (200–400 ms) after a sample moving in the preferred and the anti-preferred direction. Although the firing rates of many neurons after exposure to stimuli moving in the two directions were not significantly different (grey circles), there was a large group of cells with activity that depended on the direction of the preceding sample (yellow and blue circles; *t*-test $p > 0.05$). **c** | Receiver operating characteristic (ROC) analysis of firing rates recorded during the delay. The delay was divided into 7 independent 200-ms periods. Values significantly different from 0.5 indicate firing rates that carry directional signals³⁵. Two populations of cells that signal sample direction were identified: cells with higher firing rates after the preferred direction (blue) and cells with higher rates after the anti-preferred direction (yellow). **d** | The proportion of neurons contributing to the curves shown in **c**. More cells showed a significant ROC score after the anti-preferred sample. Data from REF. 35 © (2000) American Physiological Society.

ROC
(Receiver operating characteristic). ROC analysis, introduced in signal detection theory, is often used to evaluate the results of a detection task with weak signals. A ROC curve is generated by plotting the probability of true positives (hits) against the probability of false positives (false alarms) for a binary classifier system as its criterion is varied. In neurophysiology, it is used to test whether an ideal observer could reliably identify a given stimulus (such as direction of stimulus motion) or a behaviour based on a neural response (such as firing rate).

N-BACK TASKS
The subject is presented with a series of stimuli and is required to respond when the stimulus on the current trial matches that presented *n* trials ago. The memory load can be increased by increasing *n*. The subject has a dual task: to encode the current stimulus and to compare it with that presented on the *n*-to-last trial.

of the test stimulus. Analysis of the activity that was recorded during the delay revealed significant differences in firing rates with respect to the direction of the preceding sample. Early in the delay, about 300 ms after sample offset, a large proportion of neurons had significantly higher firing rates after a stimulus that moved in the anti-preferred direction (yellow circles; FIG. 3b) and a smaller proportion fired significantly more after a stimulus that moved in the preferred direction (blue circles). ROC (receiver operating characteristic) analysis of firing rates recorded during this period and during the rest of the delay revealed the presence of reliable directional signals: most neurons fired more after the preferred direction, whereas a small proportion of neurons fired more after the anti-preferred direction (FIG. 3c,d). So, throughout the delay, the direction of the remembered stimulus was represented in area MT, consistent with the idea that this sensory region of cortex participates in the retention of visual motion information^{15,20}.

Imaging. The use of functional imaging to study the neural correlates of perceptual memory has been discussed in previous reviews^{36,37}. Here, we highlight studies that focus on the involvement of sensory cortical areas in visual working memory. These studies also support the view that sensory cortical areas participate in working memory, although the results seem to depend on the type of working memory task that is used. For example, imaging studies show greater memory-related activity in sensory cortex during delayed discrimination tasks than during *N-BACK TASKS*. During a delayed discrimination task that involved spatial frequencies, there was a delay-related increase in activity not only in the prefrontal and posterior parietal cortex but also in the occipital cortex, which processes visual information³⁸. Similarly, delay-related increases in visual cortical activation occurred during delayed discrimination of stimulus orientations³⁹. However, studies that used *n*-back tasks reported strong activation

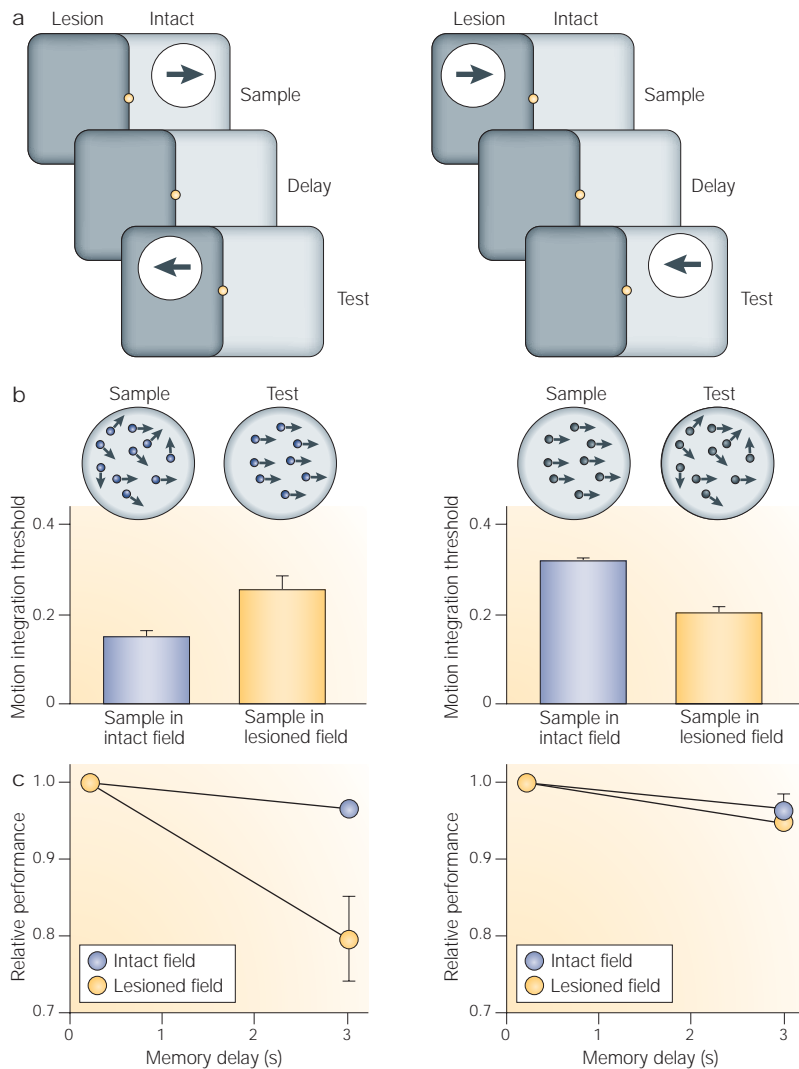


Figure 4 | Effect of MT/MST lesions on discrimination and memory of the direction of complex motion. **a** | Monkeys with unilateral MT/MST lesions performed the task with sample and test stimuli in opposite hemifields so that one was placed in the lesioned hemifield and the other in the corresponding location in the intact hemifield. **b** | Normalized direction range thresholds (360 -range threshold/ 360) measured when the delay between sample and test was minimal (0.2 s). The sample or the test stimulus was composed of dots moving in a range of directions (blue), whereas the other contained only coherent motion. ‘Sample in intact field’ (blue) indicates that the sample was presented in the intact visual field and that the test was presented in the lesioned hemifield. ‘Sample in lesioned field’ (yellow) indicates that the sample was presented in the lesioned hemifield and that the test was presented in the intact hemifield. Thresholds were poorer whenever the stimulus containing non-coherent motion was placed in the lesioned field. **c** | Effect of delay on performance for two direction range tasks. Thresholds were measured with both stimuli in the intact (blue circle) or lesioned (yellow circle) hemifield. Range thresholds were measured either by varying the range of directions in the sample while the test moved coherently (left graph) or by varying the range of directions in the test while the sample moved coherently (right graph). Thresholds were normalized to the data measured at 0.2 -s delay. Error bars show SEM. A delay-specific deficit was present only when the remembered stimulus (sample) contained a broad range of directions and required integration. Modified, with permission, from REF. 15 © (2000) Oxford University Press.

mainly in regions outside sensory cortex, such as the prefrontal and posterior parietal cortex, with little selective activation in visual cortex^{36,40–42}. One possible explanation for the absence of delay activation in visual cortex in *n*-back tasks is that memory representation of target and non-target stimuli used in such tasks interact, and this interaction might impede on-going cortical activity.

Lesions. One of the first studies to investigate the effects of sensory cortical lesions on working memory was performed by Fuster and colleagues, who applied local cooling to IT cortex in monkeys during a DELAYED MATCH-TO-SAMPLE task⁴³. Cooling produced severe impairments in performance, but only when there was a long memory delay between the sample and test stimuli. In a subsequent study⁴⁴, Fuster *et al.* examined the effects of cooling of the dorsolateral PFC on the performance of the same task and on the activity of neurons in IT. Cooling affected task performance and altered the stimulus selectivity of neuronal activity in IT during the delay period. These results show that interactions between prefrontal and IT neurons probably have an important role in working memory. The role of IT cortex in retaining information about visual objects or colour has been confirmed by other lesion studies^{45,46}, providing physiological evidence for the involvement of IT cortex in visual working memory.

As described above, neurons in area MT carry signals about the remembered direction during a memory-formation task³⁵. The involvement of area MT in working memory has also been documented in a lesion study¹⁵. The authors used the same memory task and investigated the effects of unilateral lesions of area MT and the neighbouring area MST (both areas of extrastriate cortex that are involved in processing visual movement). By placing either a sample stimulus or a test stimulus in the intact or lesioned visual hemifield, they could assess separately the contribution of this area to the encoding and storage of visual motion. When the sample stimulus consisted of random dots moving in a broad range of directions (complex motion), MT/MST lesions disrupted both encoding of these stimuli and their retention at a longer delay (FIG. 4). However, when a coherent sample (all dots moving in the same direction) was displayed in the lesioned visual hemifield, there was no deficit in perceptual thresholds and no additional deficit with a longer delay. This result showed that encoding and storage seem to be closely linked; when the lesion affected stimulus encoding, retention of that stimulus was also degraded.

Investigations in patients with focal brain damage also support the involvement of regions that process sensory information in visual working memory. The short-term retention of spatial frequency⁴⁷, speed of motion⁴⁸, colour^{49,50} and complex spatial patterns⁵¹ is impaired by focal lesions in the associational occipito-temporal cortical areas that are known to be involved with the encoding of these stimulus features. Memory-guided saccades are less accurate in patients with damage to the occipito-parietal cortex and the PFC^{52,53}, which are involved in the control of saccadic eye movements in monkeys. In the study shown in FIG. 5, 23 patients with surgical resections of temporal or parietal cortex performed simultaneous and delayed speed-discrimination tasks. Patients with damage to the left superior temporal cortex, and in particular the lateral superior temporal cortex (FIG. 5b), showed impaired speed discrimination as well as reduced memory for stimulus speed. The lateral superior temporal cortex in humans corresponds

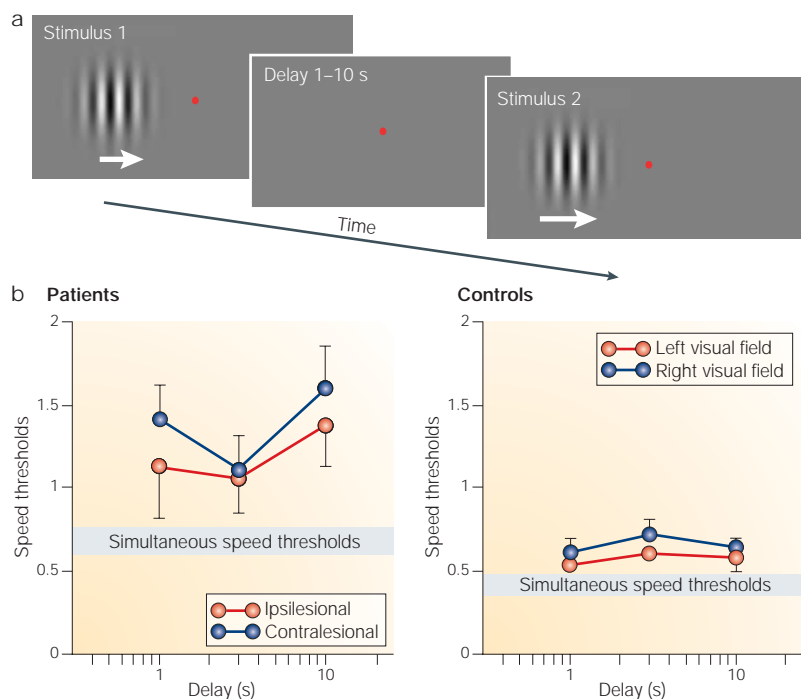


Figure 5 | Sensory working memory in patients with focal brain lesions. In this study⁴⁸, the effects of brain lesions on the delayed discrimination of stimulus speed were assessed. **a** | Experimental design used to assess speed memory. The sample and test stimuli moved in the same direction but could differ in speed, and were separated by a 1–10-s delay. **b** | Results of delayed discrimination tasks for patients with lesions in the superior temporal cortex (left), as compared with the results of age-matched controls (right). Grey shaded region denotes the mean value ± 1 SEM of simultaneous (left versus right) speed discrimination thresholds. Although the patients showed slightly elevated thresholds in the simultaneous task, their thresholds rose sharply with increasing delay duration. The effect is more pronounced for stimuli presented in the visual field contralateral to the brain-damaged hemisphere.

approximately to area MST in the extrastriate cortex of macaque monkeys, and similar impairments have been reported in monkeys with damage to the motion-sensitive MT/MST region⁵⁴. These results support a role for extrastriate and associative visual cortex in the short-term storage of velocity information.

Stimulation. Bisley *et al.*²⁰ found that microstimulation of direction-specific cortical columns in area MT of monkeys that were performing a memory-for-visual-motion task affected performance during both encoding and retention. However, the nature of these effects depended on the phase of the task during which the stimulation was delivered (FIG. 6).

Stimulation applied during presentation of the sample caused performance to drop to significantly below chance levels. Further analysis revealed that on these trials the monkeys nearly always identified the direction of the sample as that preferred by the stimulated column, irrespective of the actual sample stimulus. So, stimulation during the sample produced signals that were interpreted by the monkeys as directional motion. Stimulation during the delay period also affected performance, but the signals it produced were disruptive, bringing performance to chance levels. The effects of microstimulation during visual stimulation showed

that the directional information used by the monkeys in the task was provided by neurons in area MT. The disruptive effects of stimulation during the delay indicates that MT neurons also participate in the storage of visual motion information, either by being connected to the storage circuitry or by being an integral component of that circuitry.

TRANSCRANIAL MAGNETIC STIMULATION (TMS) has also been used to examine the contribution of cortical areas that process sensory information to working memory in humans. For example, when TMS was used to disrupt activity in human area MT, motion PRIMING was eliminated⁵⁵. As this effect was specific to visual motion and to area MT, the authors concluded that priming for basic stimulus attributes depends on the intermediate stages of cortical visual processing. A recent psychophysical study of priming⁵⁶ confirmed that idea.

Tactile working memory

Psychophysics. Early studies showed that tactile information (for example, for three-dimensional shapes, location and duration of stimulation) can be preserved for up to 80 s even when intervening tasks prevent rehearsal^{57,58}. In a more recent study, Sinclair and Burton⁵⁹ found that, although subjects could perform delayed discrimination of vibration stimuli with delays of many seconds, the accuracy of this discrimination was maximal at short delays and decreased rapidly during the first 5 s of the delay. During longer delays, performance did not continue to deteriorate, indicating that a two-stage memory process might be involved. Monkeys can also accurately retain information about vibratory stimuli for many seconds⁶⁰.

These studies reveal that, like visual stimuli, the remembered tactile stimuli are faithfully represented in working memory. This indicates that the regions that encode tactile information might be needed for this representation to persist during the memory delay.

Physiology. The work of Romo and colleagues provided some of the most compelling evidence in support of the involvement of somatosensory cortical neurons in working memory tasks. They recorded neuronal activity in cortical areas SI and SII during a delayed discrimination task that involved mechanical vibration (flutter) applied to a monkey's fingertip^{61,62}. The monkey had to judge which of two stimuli separated by a delay had the higher frequency. The authors found no delay activity in area SI (REF. 63). However, in area SII (the subsequent processing stage), about a third of neurons that were significantly modulated by stimulus frequency continued to fire for several hundred milliseconds into the 3-s delay. Furthermore, their responses to the second stimulus contained information about the remembered stimulus, reflecting the relationship between the two stimuli, which was the problem that the monkey was asked to solve⁶⁴. Romo and his colleagues also recorded the activity of other cortical areas, including premotor and prefrontal regions, during the same task. These studies provided a unique insight into the circuitry that underlies the performance of a tactile working memory task (see below).

DELAYED MATCHING-TO-SAMPLE TASKS

Presentation of a stimulus is followed by a delay, after which a choice is offered. In matching tasks, the original stimulus that was presented must be chosen; in non-matching tasks, a new stimulus must be selected. With small stimulus sets, the stimuli are frequently repeated and become highly familiar. So, such tasks are most readily solved by short-term or working memory rather than by long-term memory. In the original version of this task, trained animals or instructed volunteers report whether two stimuli separated by a memory delay are the same or different.

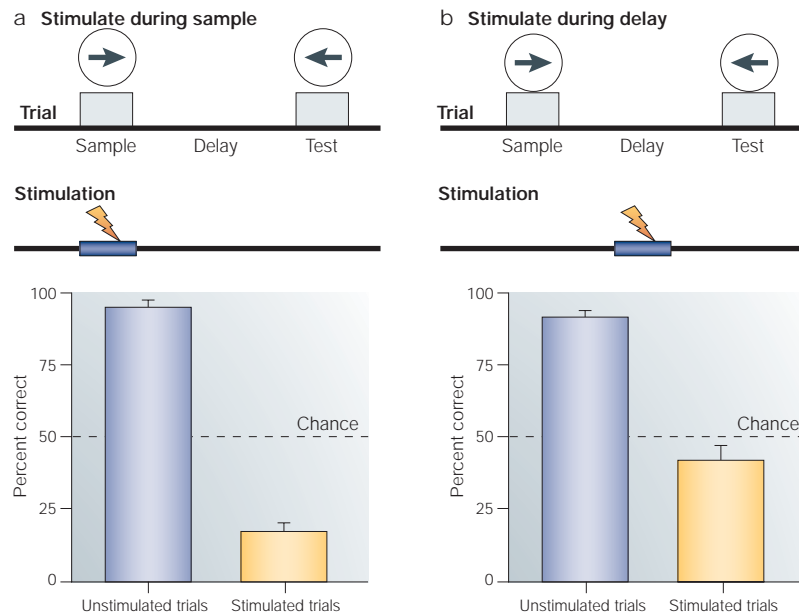


Figure 6 | Effect of electrical microstimulation of area MT on memory for motion. The timing of the sample, test and electrical microstimulation are shown diagrammatically (top). Microstimulation (80 mA, biphasic 200 Hz; 500 ms duration) of identified directional columns in MT was applied on 25% of trials chosen at random and was either coincident with the presentation of the sample stimulus (a) or was applied during the delay (b). The two conditions were presented in separate blocks of trials. When microstimulation was applied during the sample, the performance dropped to 15% correct (a). Further analysis revealed that the animals consistently reported that the sample moved in the direction preferred by the stimulated cluster of neurons, showing that the signal produced by the microstimulation was interpreted as visual motion. When the same microstimulation was applied during the delay, it no longer produced consistent directional signals; the performance dropped to near chance. These effects indicate that MT neurons participate in storage of motion information by either maintaining an active connection with the circuitry involved in storage or by being an integral component of that circuitry. Modified, with permission, from REF. 20 © (2001) American Physiological Society.

Although these studies found no memory-related activity in area SI, experiments by Fuster and colleagues did. These studies reported stimulus-related delay activity in neurons in SI and in other regions that have been implicated in texture analysis in monkeys that were trained on a memory task involving texture discriminations^{23,65}.

Imaging. Several imaging studies have focused on the ability to recognize and remember objects on the basis of tactile input⁶⁶. For example, positron emission tomography (PET) studies have shown activation in the parietal operculum (area SII), an associative somatosensory area, during working memory tasks that use vibratory stimuli⁶⁷ or palpated wire forms⁶⁸. As a rule, these activations were accompanied by increased activity in other cortical regions, including the dorsolateral PFC. Information gained by tactile palpation of objects can be stored in working memory and used for discriminations. In a sequential discrimination task⁶⁹, functional magnetic resonance imaging (fMRI) showed delay-related activity in the PFC, frontal operculum and anterior parietal cortex. This activity could reflect the maintenance of non-visual object information over the delay period. Interestingly, there is considerable overlap between the prefrontal activations for tasks that

involve haptic object encoding and those that involve visual encoding. Perhaps three-dimensional object information is extracted and stored in a supramodal fashion to allow recognition based on information flowing in from the different senses. In this manner, working memory would assist early-level sensory processes to form mental representations of objects that are explored in more than one sensory domain.

Transcranial magnetic stimulation. TMS has also been used to investigate the neuronal basis of memory for vibration frequency. When subjects were asked to compare the frequencies of two vibrations that were separated by a 1.5-s delay, TMS applied to area SI on the contralateral side in the early phase of the retention period increased the threshold for discrimination, whereas TMS later in the delay did not⁷⁰. The authors concluded that area SI processes and stores vibration information, directly contributing to working memory. Physiological recordings from areas SI and SII in monkeys support this idea (see above).

Auditory working memory

Psychophysics. Humans can accurately discriminate the pitch and loudness of sounds⁷¹, and our auditory working memory can persist for many seconds⁷². Like experiments on visual working memory, auditory memory studies also use interfering stimuli during the memory delay to investigate the nature of remembered stimuli. For example, memory for pitch can be disturbed by distractor tones, but only if the tones are within a narrow range of frequencies relative to the frequency of the remembered stimulus, supporting the hypothesis that there are separate pitch memory modules with inhibitory interactions^{73,74}. In an auditory memory task, discrimination thresholds for pitch and loudness decline at different rates with increasing delay⁷⁵ — intensity discrimination decreases more rapidly than frequency discrimination, indicating that pitch and loudness are processed separately in auditory memory. The differences in the precision of memory for intensity and pitch are parallel to the findings in vision for contrast and spatial frequency (see above). Furthermore, there is evidence that sound frequency is stored separately from location information^{76,77}. These findings indicate that, like visual memory, auditory memory involves separate stores for important physical parameters of the remembered stimuli.

Physiology. To study neuronal activity in the auditory cortex, Gottlieb *et al.*⁷⁸ trained a monkey to compare two pure tones separated by a brief memory delay. During the delay, the firing rates of many neurons reflected the frequency of the first tone. In addition, in a subset of neurons, responses to the second tone depended on whether its frequency matched that of the first. These results strongly implicate auditory cortex neurons in the circuitry that underlies working memory for tone frequency. The participation of the auditory cortex in auditory working memory is also supported by a MAGNETOENCEPHALOGRAPHY study that investigated memory for tone loudness⁷⁹. In addition, the auditory

TRANSCRANIAL MAGNETIC STIMULATION

A technique that is used to induce a transient interruption of normal activity in a relatively restricted area of the brain. It is based on the generation of a strong magnetic field near the area of interest, which, if changed rapidly enough, will induce an electric field that is sufficient to stimulate neurons.

PRIMING

The facilitation of recognition, reproduction or biases in the selection of stimuli that have recently been perceived.

Box 2 | Computational models of working memory

Interactions between the prefrontal cortex (PFC) and sensory areas have been incorporated into biophysically based models that are designed to account for persistent activity in the PFC^{95,108}. In one class of models, a working memory network is characterized by multiple attractor states, each of which retains a representation of a stimulus to be remembered¹⁰⁹. Sensory information is fed into a network of neurons that are involved in parametric storage of analogue stimulus dimensions such as spatial location or tactile vibration, and this storage is mediated by a neural assembly that has a resting state at low firing rates and a self-sustaining 'attractor' state at elevated firing rates. Such 'attractor' models have provided a realistic account of several types of delay activity that have been recorded in the PFC^{110,111} and inferotemporal cortex¹⁰⁹. One of the features of such recurrent networks is that they are likely to be disrupted by distractors that resemble the stimulus retained by such networks¹¹⁰. This behaviour is reminiscent of the 'memory masking' that is observed in psychophysical experiments (FIG. 2).

MAGNETOENCEPHALOGRAPHY

A non-invasive technique that allows the detection of the changing magnetic fields that are associated with brain activity. As the magnetic fields of the brain are weak, extremely sensitive magnetic detectors known as superconducting quantum interference devices — which work at very low, superconducting temperatures (–269 °C) — are used to pick up the signal.

cortex is connected to regions in the PFC⁸⁰ that have been implicated in working memory (BOX 1), which further supports the involvement of this key sensory region in the retention of auditory stimuli.

Imaging. Several imaging studies have focused on the ability to remember differences in pitch and tonal sequences. In these studies, tonal sequences produced memory-related activity in associative auditory cortex in the right superior temporal lobe, and pitch judgements were associated with increased activation in the right frontal lobe^{81,82}. There is also evidence that the activation in the auditory cortex is greatest early in the delay, whereas regions in the supramarginal gyrus and parts of the cerebellum are activated later, indicating that these areas have different roles in memory for pitch⁸³.

Lesions. Patients with damage to auditory associative cortex in the right temporal lobe show selective deficits in short-term storage of auditory information. These patients are unimpaired on a tone discrimination task with a short (1.65-s) delay, but show deficits when a longer delay with an interfering tone sequence is introduced⁸⁴.

Conclusions

We have reviewed the evidence that the circuitry that underlies working memory for sensory signals is likely to include cortical areas that are devoted to the processing of these signals. This conclusion is supported by the results of a wide range of studies, from purely perceptual measurements to recordings from single cells and functional imaging. Manipulations such as lesions and stimulation provide further confirmation of this hypothesis, which is also supported by computational modelling (BOX 2).

One of the difficulties we encountered while reviewing this evidence was the difference in the treatment and analysis of sensory stimuli used in memory tasks. Studies that use exclusively psychophysical approaches tend to focus on the precise nature of the sensory representation, carefully manipulating stimuli used in memory tasks along a well-defined sensory dimension. For example, visual psychophysical studies indicate that information about stimulus size (spatial frequency) is likely to be preserved by distinct, narrowly tuned mechanisms, and that information about the motion of random dots is preserved with information about its precise speed and location. Similarly, investigations of auditory working memory have provided evidence that information about pitch, loudness and location is preserved by separate, narrowly tuned mechanisms.

On the other hand, single-cell recording studies have focused largely on the nature of memory-related neural activity and its localization in the cortex. Although such studies have provided invaluable insights into the nature of neural activity during the performance of working memory tasks, few have shed light on how this activity represents the remembered sensory stimuli. Among studies that have focused on the nature of sensory representation are those by Romo and colleagues^{61–64}. By parametrically manipulating a vibratory stimulus they showed that, during the memory period, information about vibration frequency was preserved not only in area SII but also in the PFC and the premotor cortical area, shedding light on the circuitry that underlies working memory in this task.

The main strength of brain imaging studies is their ability to reveal simultaneous activation of multiple cortical regions during working memory tasks. These studies lend further support to the role of mid-level sensory areas that interact with the PFC and the parietal cortex during these tasks. However, with few exceptions, these studies have mainly produced evidence for a coarse subdivision of 'what' and 'where' aspects of information processing. Like single-cell recordings, imaging studies of sensory working memory would benefit from attempts to focus on more specific aspects of the stimulus material being remembered, to support or reject the theory of feature-specific memory stores.

Although the participation of sensory cortical areas in the circuitry that temporarily stores sensory information is well documented, the precise nature of this participation is still unclear. We believe that to understand how the brain deals with this important problem, we must devote more attention to exactly what is remembered.

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Competing interests statement

The authors declare no competing financial interests.

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