Perceptual–mnemonic functions of the perirhinal cortex

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It is widely acknowledged that the perirhinal cortex, located in the ventromedial aspect of the temporal lobe, is essential for certain types of memory in macaque monkeys. For example, removal of the perirhinal cortex yields severe impairments on tests of stimulus recognition and stimulus–stimulus association. There is considerable disagreement, however, about the most accurate way to characterize the function of the perirhinal cortex; some views emphasize a role in perception whereas others posit a role exclusively in declarative memory. In this article, we review recent findings from anatomical, physiological and ablation studies in monkeys, and discuss related findings obtained in humans, in an attempt to identify not only the cognitive functions of the perirhinal cortex, but also the implications of these findings for theoretical views concerning the organization of memory.

T he perirhinal cortex (Brodmann's cytoarchitectonic areas 35 and 36) is a region located in the ventromedial aspect of the temporal lobes (see Box 1). In macaques, this narrow strip of cortex occupies the lateral bank of the rhinal sulcus and continues onto the laterally adjacent gyrus. The region extends from the face of the temporal pole, rostrally, to cover much of the inferior temporal gyrus, caudally. The last decade has seen an explosion of findings concerning the anatomy and function of the perirhinal cortex. (A search of the Medline database revealed 312 papers on the subject from 1988 to the present, in primary publications alone, with untold numbers of chapters and reviews besides, relative to the 59 papers found in the two decades spanning 1966–1985.) This heightened interest is due, in part, to the assignment of a function to the perirhinal cortex. That is, although the perirhinal cortex has long been known to exist, only in the last decade has it been assigned a putative function – what initially appeared to be a selective role in visual recognition memory (see Box 2). In addition, however, it has become clear that the perirhinal cortex is much more important than the hippocampus for some mnemonic functions, and this realization, too, has justifiably led to increased interest in this cortical field.

In this article, we review and synthesize findings from anatomical, physiological, and ablation studies carried out in nonhuman primates in an attempt to elucidate the cognitive functions of the perirhinal cortex, as well as the implications of these findings for theoretical views concerning the organization of memory.

Role of the perirhinal cortex in recognition memory
As previously mentioned, the recent dramatic rise in interest in perirhinal cortex has been due in part to the assignment of a function – what appeared initially to be a central and perhaps selective role in stimulus recognition. Recognition memory in monkeys is usually assessed using the delayed nonmatching-to-sample (DNMS) procedure. In this task, each trial is composed of two parts, sample presentation followed by choice test. The rule for DNMS is 'if sample **A**, then choose **B** but not **A** on the choice test', where **A** and **B** represent 3-D objects presented on a test tray or 2-D visual stimuli presented on a touch-sensitive monitor screen. [In the matching-to-sample (DMS) task, animals must choose the matching, or 'sample', item on the choice test.] After the DNMS/DMS rule has been mastered, recognition memory abilities typically are evaluated by: (1) increasing the delay intervals interposed between the sample presentation and choice test, and (2) increasing the number of items to be remembered.

In 1987, Horel et al.[1] found that ablation or cooling of the inferior temporal gyrus of macaques, much of which is occupied by the perirhinal cortex (see Box 1), led to severe impairment on DMS. Zola-Morgan and colleagues[2] then showed that removal of the perirhinal cortex together with the parahippocampal cortex (areas TF and TH) produced a severe impairment in both learning the DNMS rule, and in performing DNMS when long delays were interposed between sample and choice. In addition, Murray and colleagues[3–5] reported that combined lesions of the entorhinal and perirhinal cortex led to severe impairments in learning and performance on DMS and DNMS tasks. Finally, Meunier et al.[5] showed that lesions limited to the perirhinal cortex yielded a recognition deficit almost as severe as that which follows the combined removal of the entorhinal plus perirhinal cortex, and, notwithstanding the difficulty of

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Box 1. Where is perirhinal cortex?

Lateral and ventral views of the macaque brain are shown in the upper and lower parts of Fig. I (**A–D**), respectively. (**A**) In monkeys, the inferior temporal gyrus (ITG) and middle temporal gyrus (MTG), which lie either side of the anterior middle temporal sulcus (amts), together comprise the inferior temporal, or 'IT', cortex. This region is bounded by the superior temporal sulcus (sts), dorsolaterally, and by the rhinal sulcus (rs), ventromedially. (**B**) von Bonin and Bailey's cytoarchitectonic map shows a single area, 'TE', spanning the middle and inferior temporal gyri of Old World monkeys (Ref. a). For completeness, the diagram in (**B**) also shows the location of von Bonin and Bailey's areas TF and TH, which together comprise the parahippocampal cortex. Note that other early cytoarchitectonic and myleoarchitectonic delineations (e.g. Brodmann, Ref. b), together with more modern depictions (Refs c,d) show two or more separate fields occupying IT. Nevertheless, the use of the label 'area TE' (or IT) was prevalent in neuroanatomical, neurophysiological and neuropsychological studies carried out in nonhuman primates from the 1960s to the present, and the entire expanse of IT cortex was typically regarded as a single entity. (**C,D**) The perirhinal cortex (PRh) in macaque monkeys is found at the ventromedial aspect of the temporal lobe, is comprised of Brodmann areas 35 and 36 (Ref. b), and occupies the lateral bank of the rhinal sulcus plus a substantial portion of the inferior temporal gyrus. It has the same relative location in rats and humans (Refs e,f). It is now widely recognized that the perirhinal cortex extends more laterally than depicted in early cytoarchitectonic maps (see Box 2), though there is no consensus as to the precise location of the perirhinal (PRh)–TE boundary (compare **C** and **D**). (**C**) shows the lateral boundary of perirhinal cortex at or near the fundus of the anterior middle temporal gyrus (Ref. g). (**D**) depicts the lateral boundary as roughly one-third to one-half of the distance (depending on the anterior–posterior level) between the rhinal sulcus and anterior middle temporal sulcus (Refs h–k). (TEad and TEav are anterodorsal and anteroventral subdivisions of area TE, respectively.)

That the perirhinal cortex and area TE are indeed separable subdivisions of the inferior temporal cortex was shown by Buckley and colleagues (Ref. l), who found a double dissociation of function following ablations of perirhinal cortex and middle temporal gyrus, which is coextensive with dorsal TE. Monkeys with removals of the perirhinal cortex, but not those with removals of dorsal TE, were significantly impaired on delayed nonmatching-to-sample, a measure of visual recognition memory. By contrast, monkeys with removals of dorsal TE, but not those with removals of perirhinal cortex, were deficient in their ability to discriminate colors.

Fig. I. (See text for description; part C adapted from Ref. m, part D adapted from Ref. i).

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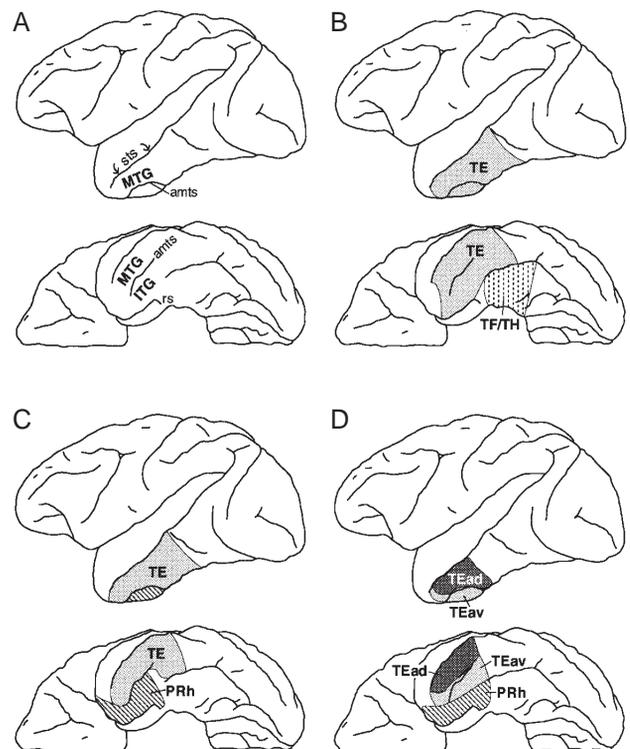**e** Burwell, R.D. *et al.* (1996) Some observations on the perirhinal and parahippocampal cortices in the rat, monkey, and human brains, in *Perception, Memory, and Emotion: Frontiers in Neuroscience* (Ono, T., ed.), pp. 95–110, Elsevier

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directly comparing data across laboratories, as that which follows removal of the perirhinal plus parahippocampal cortex[2]. The impairment after removal of perirhinal cortex holds for tactual as well as visual recognition[6]. Thus, damage to the perirhinal cortex is particularly devastating to stimulus recognition.

Physiological studies have identified at least two ways in which the activity of neurons in perirhinal and neighboring cortical fields might support stimulus recognition. First,

several studies have reported that neurons in the monkey perirhinal cortex fire fewer action potentials during the second or subsequent exposure to a stimulus relative to the first[7–10]. It is worth remarking that neurons showing this 'repetition suppression effect' are located in just those areas in the medial temporal lobe that are involved in visual recognition, namely the perirhinal cortex, entorhinal cortex and area TE, but not in the hippocampus[11]. Taken together with the evidence from ablation studies just cited, it is

Box 2. Recognizing perirhinal cortex

The inferior temporal cortex of macaque monkeys has long been known to be critical for visual perception and memory (Refs a,b). In the late 1980s, at least three major findings served to bring one small portion of the inferior temporal cortex, the perirhinal cortex, toward the forefront of neurophysiological and neuropsychological investigations of learning and memory. First, although the perirhinal cortex (i.e. areas 35 and 36 of Brodmann, Ref. c) had been identified in early cytoarchitectonic studies of marmoset monkeys, lemurs, and macaques as a field residing primarily in the lateral bank of the rhinal sulcus, more recent delineations of the extent of perirhinal cortex based on anatomical connections led Amaral and his colleagues (Refs d–f) to suggest that this region extends more laterally than previously recognized, at least in macaques (see Box 1, Fig. IC). Second, a pioneering physiological study carried out by Brown and colleagues (Ref. g) revealed that the activity of cells in the perirhinal and neighboring cortical fields of macaque monkeys reflect the animal's prior exposure to a visual stimulus. The phenomenon they reported, namely, a decrement in neuronal firing on second and subsequent viewing of a stimulus, has now been observed in several laboratories (Refs h–j) and is widely accepted as a potential neural correlate of visual recognition. Third, Horel and his colleagues (Ref. k) reported that ablation or cooling of the inferior temporal gyrus in monkeys severely disrupted visual recognition memory, as measured by the delayed matching-to-sample task. This latter finding has also been confirmed and extended in other laboratories, and is the focus of a section of this article.

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tempting to speculate that the decrement in firing is *the* neural correlate of visual stimulus recognition. There are, however, viable arguments against this idea[12,13], so the issue is presently unresolved. Another way in which perirhinal cortical neurons reflect stimulus memory is by *increased* firing on the second relative to the first viewing, a phenomenon known as the 'enhancement effect'[14]. Both of these putative short-term memory mechanisms may be operating within the perirhinal cortex and neighboring fields, depending on the task demands.

Role of the perirhinal cortex in stimulus–stimulus association

Stimulus–stimulus association is usually evaluated through the use of conditional tasks of the form 'if cue (or sample stimulus) *A,* then choose *X* but not *Y*; if cue *B,* then choose *Y* but not *X*'. In conditional tasks, unlike the matching tasks, the sensory modality of the instruction cue (*A* or *B* in the example above) may or may not be the same as that for the choice. For example, an auditory cue might instruct the choice of a particular stimulus based on its visual features (auditory–visual conditional task) or a visual stimulus might instruct the choice of another stimulus based on its visual features (visual–visual conditional task).

Recent evidence suggests that the same regions involved in stimulus recognition are also important for certain types of stimulus–stimulus association. For example, removals of

the entorhinal and perirhinal cortex together[15] or of the perirhinal cortex alone[16] lead to severe deficits in the learning of visual–visual conditional problems. In addition, Parker and Gaffan[17] have found that combined removals of the entorhinal and perirhinal cortex severely disrupt flavor–visual associations. Moreover, Goulet and Murray[18] have preliminary results indicating that damage to the entorhinal and perirhinal cortex disrupts tactual–visual associations. Finally, indirect evidence suggests that the perirhinal cortex is likely to be critical for retention and relearning of auditory–visual conditional problems as well[19]. Thus, the perirhinal cortex appears to be important for relating together the different sensory features of particular objects, thereby facilitating object identification. Because the perirhinal cortex is the first cortical field in the ventral visual stream that receives inputs from all the higher-order, modality-specific neocortical fields (see Box 3), its unique 'associative' function may be largely a reflection of its anatomical relations, as opposed to any special information processing function.

Physiological studies have identified several mechanisms that may mediate stimulus–stimulus associations. For example, Miyashita and his colleagues[20,21] have reported two kinds of activity, recorded from neurons in the anterior inferior temporal cortex including perirhinal cortex, that may reflect association memory. In their experiments, monkeys were trained on the same type of visual stimulus–stimulus association task described above. They found that, following

Box 3. What brain areas are connected to perirhinal cortex?

The anatomical connections of the perirhinal cortex distinguish this portion of the inferior temporal cortex from the remainder. There are two striking features of perirhinal cortex connectivity (see Fig. I). First, although it has been estimated that roughly 60% of the cortical inputs to perirhinal cortex are from visual areas (Ref. a), the perirhinal cortex also has interconnections with sensory cortical fields serving non-visual modalities. For example, the perirhinal cortex receives projections from modality specific cortical fields, such as the posterior two-thirds of the insula devoted to somatosensory processing (Refs a,b) and some superior temporal cortical fields devoted to auditory sensory processing, as well as those from TE and TEO devoted to visual sensory processing (Ref. a). In addition, the perirhinal cortex receives projections from several regions that might be considered multimodal, such as the cortex of the parahippocampal gyrus and the orbital frontal cortex (Refs a,c). Thus, the perirhinal cortex is the first cortical field within the ventral visual processing stream in which there is convergence of information from different sensory modalities. A second remarkable feature of perirhinal cortical connectivity is that the region is in a pivotal location to relay processed information to other structures thought to be critical for certain types of associative memory. The perirhinal cortex has heavy connections with the amygdala, the hippocampus (mainly indirectly via the entorhinal cortex), the striatum, and with the same neocortical fields, outlined above, from which it also receives projections (Ref. d).
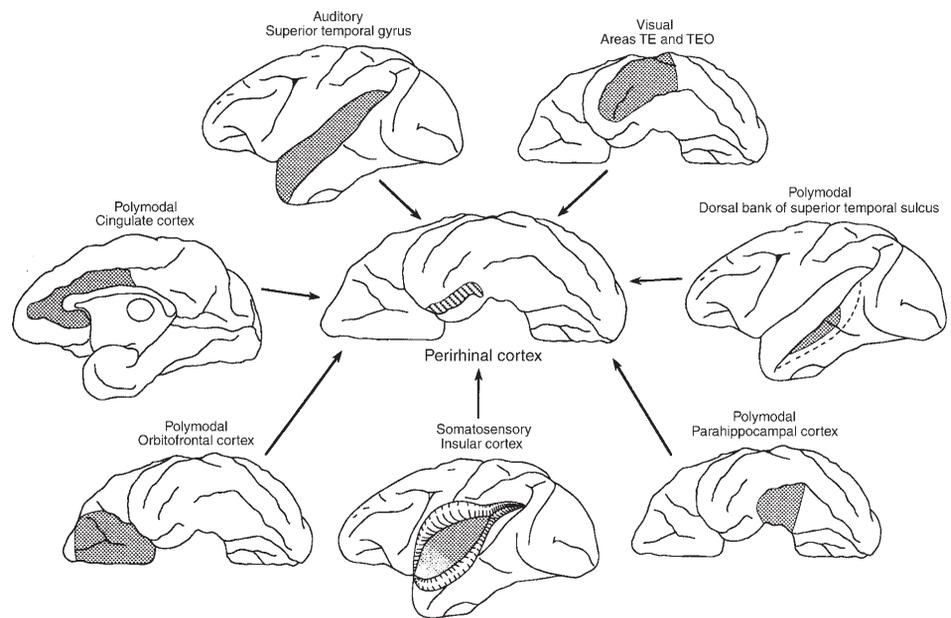

Fig. I. Afferent connections of the perirhinal cortex. Schematic diagrams of the lateral or ventral view of the macaque brain showing the main cortical fields that contain neurons projecting directly to the perirhinal cortex (center). (Adapted from Ref. d.)

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training, some neurons had responses of a similar magnitude to separate presentations of items that had been paired with one another repeatedly (i.e. to items that were 'paired associates' in the task), and that this occurred more often than would be expected by chance. In addition, they found neurons that, during the delay period between sample and choice, showed activity that reflected not the stimulus just seen, but the upcoming stimulus that should be selected on the choice test. Cells such as these, termed 'pair-coding' neurons and 'pair-recall' neurons, respectively, could well represent the stimulus–stimulus associations learned in the task, and thereby guide task performance. A later study by Higuchi and Miyashita[22] provided even more direct evidence of perirhinal cortex involvement in visual paired-associate learning. In their study, the monkeys sustained a transection of the anterior commissure, an operation that prevented the inferior temporal regions of the two hemispheres from communicating with each other, plus a lesion of the perirhinal and entorhinal cortex in one hemisphere. The monkeys had been trained on sets of visual stimulus–stimulus associations both before and after surgery. Whereas neurons in the ipsilateral TE maintained stimulus selectivity after the perirhinal and entorhinal cortex lesion, pair-coding

effects were lost. These authors concluded that interaction of perirhinal cortex and TE was essential for the emergence and maintenance of mechanisms that underlie the learning and retention of visual stimulus–stimulus associations.

Even more recently, Liu and Richmond[23] observed neuronal firing in perirhinal cortex that appears to code the relationship between the proximity of a visual stimulus to impending reward, and the behavioral context (trial type) during which the stimulus is presented. These authors trained monkeys to complete one, two, or three trials to obtain reinforcement. On each trial a visual cue indicated progress through the schedule. The activity of neurons in perirhinal cortex, but not that of neurons in the neighboring area TE, reflected the meaning of this cue with respect to progress through the schedule. For example, perirhinal cortex neurons discriminated between conditions in which the monkey was performing the last of a one-trial schedule versus the last of a three-trial schedule, even though the visual cues in the two situations were identical, and even though both trials led to delivery of reinforcement. These findings are significant, as they appear to extend the role of perirhinal cortex from the coding of relatively simple stimulus relationships such as stimulus–stimulus associations, to

the assignment to a stimulus of more complex levels of meaning.

The findings reviewed above suggest that the perirhinal cortex mediates the storage of information about objects both in the short and intermediate term, as evidenced by the DMS and DNMS tasks, as well as in the long term, as evidenced by the stimulus–stimulus association or conditional tasks. As noted elsewhere[24], the associative mechanisms outlined above could underlie not only the intramodal and crossmodal associative abilities of monkeys mentioned earlier, but also the phenomenon of 'object invariance', the ability to identify an object regardless of viewing angle, size, location of the image on the retina, and so on. It thus appears that, in these various ways, perirhinal cortex contributes to a network that contains 'factual' information about objects, including (1) relationships between visual and other visual and non-visual stimuli, (2) objects' reward histories, and perhaps (3) responses appropriate to particular objects. Because this information is often acquired across many sessions, thereby making irrelevant the events surrounding any individual learning session, this information may be more akin to context-independent semantic memory than to context-dependent episodic memory. Indeed, evidence from the ablation and physiological studies reviewed in this section has led to the proposal that the perirhinal cortex is the core of a system specialized for storing knowledge about objects, analogous to a semantic memory system in humans[24–26].

The role of perirhinal cortex in visual information processing

The previous sections reviewed evidence in support of a role for the perirhinal cortex in object recognition and in stimulus–stimulus associative memory. Several findings, however, point to a more general role for the perirhinal cortex in visual information processing. For example, Eacott and colleagues[4] reported that monkeys with combined lesions of the perirhinal and entorhinal cortex were impaired on a version of DMS using a large number of stimuli, but not on a version using a small number (two) of stimuli. Similarly, Buckley and Gaffan[27] found that monkeys with perirhinal cortex lesions were impaired in learning large but not small numbers of discrimination problems concurrently (but see Buffalo *et al.*[28] for a preliminary account of some alternative evidence). Neither of these findings can readily be understood as deficits in recognition or stimulus–stimulus association memory, and there are additional findings, discussed below, that fall into the same category. Rather than provide an exhaustive list, we will provide just two examples of the way in which perirhinal cortex appears to be important for aspects of visual learning and memory other than recognition and stimulus–stimulus association. This will be followed by a description of a tentative model that may account for these results.

Deficits in retention

Monkeys with removals of the perirhinal cortex are impaired in retention of preoperatively-learned object discriminations[3,27,29]. This result cannot be explained as an impairment in recognition memory because all objects available

for choice are equally familiar; nor can the deficit be explained as a case of impaired stimulus-stimulus associative memory, because performance requires only that stimuli be associated with reward, not that stimuli be associated with each other. Remarkably, the same animals that are impaired in retention are able to learn new discrimination problems as rapidly as controls[3,29], showing that the retention deficit is not due to a general inability of these animals to discriminate visual stimuli.

Deficits in configural learning

Another effect not easily captured by recognition or simple associative accounts is that perirhinal cortex lesions can disrupt 'configural' learning. In such tasks, animals cannot learn simply that certain stimuli are rewarded while others are not, but instead must learn the significance of *combinations* of stimuli or of stimulus features. One example of a configural task is the biconditional discrimination task, in which monkeys are required to discriminate between items **AB**+, **BC**−, **CD**+, and **AD**−. [In this schematic, stimulus features are represented by the letters **A**, **B**, **C**, and **D**, objects by the conjunction of two of these features (e.g. **AB**), reinforcement by +, and nonreinforcement by −.] Buckley and Gaffan[16], using an extended version of the biconditional task, have shown that monkeys with lesions of perirhinal cortex are significantly impaired in this type of configural learning.

The foregoing findings thus suggest a role for the perirhinal cortex beyond stimulus recognition and association. Yet how can we make sense of these disparate effects of lesions of the perirhinal cortex? How can we understand the deficit in retention of preoperatively learned discrimination problems in the face of intact learning of new problems? And why do lesions of the perirhinal cortex disrupt the learning of configural discrimination problems but not the more typical simple discrimination problems?

A tentative model

One possibility is that such results might be at least partially explained by considering the organization of visual representations in this region. Here we consider the idea that perirhinal cortex neurons represent the conjunctions of features of visual stimuli – perhaps resulting in a 'gestalt' representation of a complete stimulus – whereas regions earlier in the visual processing stream contain neurons that represent simpler features from which these complex conjunctions are formed. Such a view is well supported by anatomical and electrophysiological data, which suggest a hierarchical organization of visual information processing in the ventral visual stream. That is, as one proceeds rostrally in the ventral stream, neurons code stimulus representations of increasing complexity[30] (Fig. 1). Although the defining properties of representations in these regions have not been precisely identified, the approximate levels of complexity of such representations are reflected in the kinds of stimuli to which neurons in these regions respond[31]. This complexity appears to reach its maximum in perirhinal cortex, where neurons may represent the complex conjunction of visual features[32]. Consistent with this idea, the responses of neurons in ventral TE[33] and in perirhinal cortex (Nikos

Logothetis, pers. commun.) are highly selective for complex objects, such that reducing the complexity of a stimulus greatly reduces the cell's response. The simple features comprising the complex representations of objects in perirhinal cortex are thought to be stored in regions upstream from perirhinal cortex, such as areas TE, TEO and V4. If our supposition concerning the nature of representations in these regions is correct, a lesion in perirhinal cortex will compromise an animal's ability to represent complex conjunctions of visual features, but will leave intact the ability to represent simpler features.

The model outlined above, and the way in which it accounts for the effects of perirhinal cortex lesions, is reminiscent of Gaffan, Harrison and Gaffan's[34] distributed-trace model of IT, in which IT lesions are thought to reduce the number of 'stimulus attributes' available during visual discrimination learning. According to the present view, however, attributes of stimuli – referred to here as 'features' – are not lost following a lesion of perirhinal cortex; rather, what is lost is the ability to represent complex conjunctions of those features. This model of visual information processing within the inferior temporal cortex may go some way toward accounting for the seemingly disparate effects of perirhinal cortex removal. We now consider our two examples in turn.

Retention versus acquisition of visual discriminations

That lesions in perirhinal cortex lead more readily to retention than to acquisition deficits may be accounted for under the present view as follows. Object discrimination problems can be learned using either the representations of complex feature conjunctions or simple features alone. Under normal circumstances, the learning will be distributed across these types of representation. Thus, when the perirhinal cortex is removed following acquisition of the discrimination problems, the neurons coding the complex 'gestalt' part of the representation – a major contributor to the associative connections leading to the response – are removed. The result is an impairment in the performance of the discriminations relative to that of an intact animal. If, however, the operated monkeys are presented with a small number of new discrimination problems, the learning can readily be accomplished using the simpler feature representations alone, and there will be no difference between the operated and control monkeys in their ability to solve the discriminations.

Configural learning

The more features that a set of to-be-discriminated stimuli have in common, the more inter-item interference there will be. Representations of the complex conjunctions of features in perirhinal cortex can serve to disambiguate stimuli when feature overlap is high. Such feature overlap reaches a maximum in 'configural' tasks, in which items cannot be discriminated according to simple features. According to this view, perirhinal cortex lesions lead to deficits in configural tasks because configural discrimination problems, more so than simple discrimination problems, require representations of the conjunctions of features.

The explanatory power of this view of the organization of visual representations in perirhinal cortex has been tested
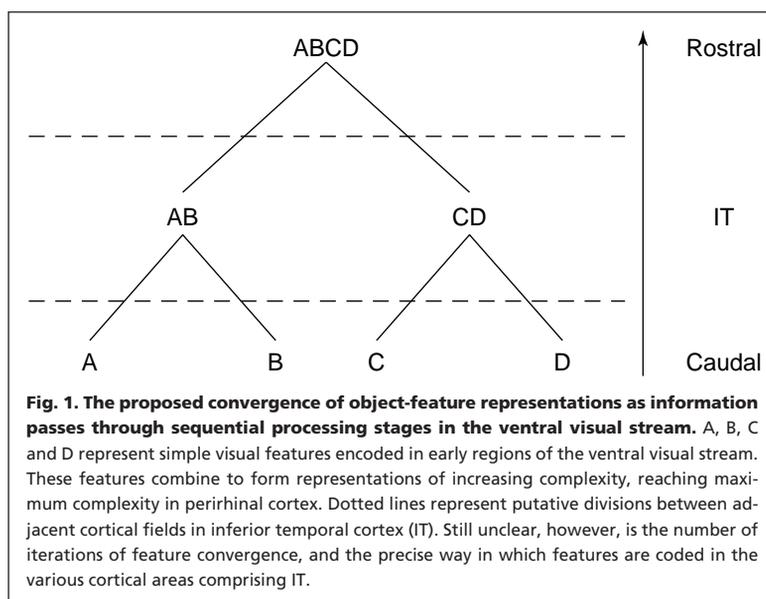

Fig. 1. The proposed convergence of object-feature representations as information passes through sequential processing stages in the ventral visual stream. A, B, C and D represent simple visual features encoded in early regions of the ventral visual stream. These features combine to form representations of increasing complexity, reaching maximum complexity in perirhinal cortex. Dotted lines represent putative divisions between adjacent cortical fields in inferior temporal cortex (IT). Still unclear, however, is the number of iterations of feature convergence, and the precise way in which features are coded in the various cortical areas comprising IT.

formally by Saksida and Bussey[35]. These authors constructed a neural network model by adding, to a base model of perceptual learning and discrimination[36], the assumption that perirhinal cortex contains representations of complex conjunctions of features, while other regions projecting to perirhinal cortex contain representations of the simpler features from which these conjunctions are formed. The network was tested in various discrimination paradigms both before and after a 'lesion' of the perirhinal cortex component. The model accurately simulated several effects of perirhinal cortex lesions in monkeys, including the adverse effects of perirhinal cortex lesions on configural learning, and the tendency for perirhinal cortex lesions to produce deficits in retention more readily than deficits in new learning. These preliminary computational results thus provide support for the view that the effects of perirhinal cortex lesions can be understood by considering its role in visual information processing.

Cognitive functions of the perirhinal cortex in humans

The perirhinal cortex in humans lies in the rostral ventromedial temporal cortex, within and along the collateral sulcus[37]. Needless to say, brain damage produced by stroke, viral infection, tumors or other agents is not likely to be restricted to this narrow strip of cortex. Furthermore, surgical resections to ameliorate epilepsy or to remove tumors typically encompass a much greater territory than the perirhinal cortex. There are, however, several findings implicating the perirhinal cortex of humans in stimulus recognition, association, and identification. With respect to recognition, Aggleton and Shaw[38] reported that amnesic patients, some of whom had sustained damage to the ventromedial temporal cortex, were impaired in recognition memory. By contrast, amnesic patients with damage restricted to the hippocampus or fornix performed relatively well on tests of recognition (Ref. 38, compare with Refs 39, 40). Consistent with this finding, Buffalo *et al.*[39] have reported that humans with extensive damage to ventromedial temporal lobe structures, including the perirhinal cortex, are deficient in visual recognition memory. In addition, as in nonhuman primates,

widespread regions of the ventromedial temporal cortex (including the fusiform gyrus, anterior medial temporal cortex and temporal polar cortex) including perirhinal cortex, show repetition suppression effects, as measured by evoked potentials[41] and functional imaging methods[42,43]. Thus, the data from humans parallel those reviewed earlier from non-human primates, and are consistent with the idea that the perirhinal cortex and neighboring regions are important for visual recognition.

There is an issue regarding recognition memory that is important to consider at this point. Some studies in monkeys[5] and humans[39] have reported that DNMS or DMS deficits are observed at long but not short delays, suggesting that the deficit is specifically in memory. That is, good performance at short delays is taken as evidence of normal perception and encoding, and, accordingly, the poor performance at longer delays is interpreted as evidence of abnormally rapid forgetting. These findings would seem to be at odds with the present view that perirhinal cortex has perceptual as well as mnemonic functions. After all, if the perirhinal cortex is important for perception, shouldn't monkeys and humans with damage to the perirhinal cortex be impaired on those conditions with short delays between sample and choice? As has been discussed in earlier sections of this article, however, damage to perirhinal cortex does not necessarily yield deficits in any and all conditions in which 'perception' is required. For example, monkeys with lesions of perirhinal cortex are able to solve small numbers of discrimination problems at a normal rate[3,29], but are impaired when required to learn large numbers of problems[27] or to learn certain configural problems[16]. Similarly, performance on DNMS or DMS with short delays will depend on task demands and the nature of the stimulus material. A striking illustration of this point was provided by Eacott *et al.*[4] Using stimuli designed intentionally to be difficult to discriminate, these authors found that monkeys with lesions of the perirhinal and entorhinal cortex were impaired on matching-to-sample under simultaneous and zero-second delay conditions. Thus, lack of an impairment on DMS and DNMS tasks with short delays cannot be taken as evidence that perception is normal.

Additional studies point to a role for the human perirhinal cortex in associative memory, especially in the processing of semantic knowledge. First, damage in the region of the ventromedial temporal cortex, including perirhinal cortex, results in semantic dementia, a condition characterized by a progressive yet relatively selective loss of knowledge about the world, including facts, concepts, and the meaning of words, together with relative preservation of visuoperceptual abilities[44]. These clinical findings, while valuable, do not speak directly to the issue of perirhinal cortex involvement, as the damage is not focal. Second, McCarthy and colleagues[45,46] have recorded a highly focal event-related potential from depth electrodes near the perirhinal cortex and from the perirhinal cortical surface of humans. The negative potential occurs approximately 400 ms after stimulus presentation, hence the name N400. The N400 is associated with anomalous sentence endings, but not with normal sentence endings, and, in addition, is larger for words with semantic content relative to words

with grammatical function. It is not elicited by nonwords or other control stimuli. Because depth electrode recordings show a reversal of the potential in the region of the perirhinal cortex, there can be little doubt but that the N400 is generated by this region. These results thus suggest that perirhinal cortex neurons are involved in processing word meaning. Third, a recent functional imaging study suggests a role for the perirhinal cortex in processing the meaning of objects. Ricci *et al.*[47] gave subjects a conceptual matching task (a variation of the Pyramids and Palms task), in which they were required to choose which one of two visually presented pictures is related to a sample picture, together with a control task, which required perceptual matching of size. The latter task was designed to be demanding so that it would provide a control not only for visual sensory processing, but also for the relatively long response latencies associated with the conceptual task. A comparison of the two conditions revealed significant activation of perirhinal cortex. Other studies[48,49] examining object or word processing and meaning have also found activations in the region of the perirhinal cortex, although these appear to be somewhat caudal to those reported by McCarthy and colleagues[46] and Ricci and colleagues[47]. Additional studies will need to address the extent to which different cortical fields in the human ventromedial temporal cortex map onto functionally equivalent cortical regions in the monkey, and how these regions contribute to semantic knowledge.

In summary, in both human and nonhuman primates, the perirhinal cortex appears to play a central role in storing and accessing knowledge about objects, and in endowing objects with meaning. Importantly, the perirhinal cortex can operate efficiently even in the absence of the hippocampus (see Box 4) and amygdala. Under normal circumstances these latter regions presumably rely on the already processed information about objects, obtained mainly via projections through perirhinal and entorhinal cortex, in carrying out their own special cognitive functions.

Perceptual versus mnemonic accounts of perirhinal cortex function

The perirhinal cortex has been considered to be part of a medial temporal lobe memory system. As such, it is often held to be important for memory but not for perception[39,50,51]. As elaborated in Box 4, this influential view suggests separate stages for perception, for which area TE is critical, and memory, for which perirhinal cortex is critical. Evidence from several sources, however, including work carried out in nonhuman primates that is reviewed in this article, suggests that the perirhinal cortex, like many other parts of neocortex, is involved in basic aspects of visual information processing. That is, although some of our claims must, at present, remain speculative, it appears that the perirhinal cortex plays a role in both perception *and* memory[52].

First, in 'perception', it serves as the final stage in a ventral visual cortical processing stream, popularly known as the 'what' pathway, that is devoted to the perception and identification of environmental stimuli[53]. Its special contribution to this type of processing is held to be in the representation of complex conjunctions of stimulus features, possibly including non-visual features as well. Second, the

Box 4. Perirhinal cortex versus hippocampus

A widely recognized and influential view holds that the perirhinal cortex is a component of a functionally unitary 'medial temporal lobe memory system', comprised of the perirhinal cortex, entorhinal cortex, hippocampus, and para-hippocampal cortex, damage to any part of which can lead to impairments in 'declarative memory' (Refs a,b). This view stands in contrast to that outlined in the present article, which argues for a role for perirhinal cortex as a processor of visual and perhaps non-visual information. In this respect the functions of perirhinal cortex are held to be more similar to those of other regions within inferior temporal cortex than they are to those of the hippocampus.

The unitary medial temporal lobe memory system view has been challenged by experiments revealing dissociations between the effects of lesions of perirhinal cortex, on the one hand, and hippocampal removal or fornix transection (which removes many of the inputs and outputs of the hippocampus), on the other. For example, whereas perirhinal cortex removal produces a severe disruption of visual recognition memory (Ref. c), as measured by DNMS and DMS tasks, excitotoxic lesions of the hippocampus that spare fibers of passage and superficial cortical fields yield either no impairment (Refs d,e; P. Rapp, pers. commun.) or an impairment much milder than that observed after perirhinal cortex damage (Refs f,g). Likewise, whereas perirhinal cortex ablations disrupt learning of visual stimulus–stimulus associations, removal of the hippocampus produces no such effect (Refs h,i). Similar dissociations have been obtained in studies in rats (Refs j–m), including those using *Fos* imaging techniques (Ref. n).

Evidence for functional double dissociations between the perirhinal cortex and fornix provides the most compelling argument against the unitary system view. In both monkeys and rats, lesions of the perirhinal cortex have been reported to disrupt object recognition abilities while sparing spatial memory abilities. Conversely, damage to the fornix disrupted spatial memory to a greater degree than object recognition memory (Refs o–r).

Additional evidence for a functional dissociation between perirhinal cortex and hippocampus is provided by studies of retrograde memory carried out in monkeys. Whereas removals of the hippocampus (plus entorhinal cortex) have a temporally limited effect on retrograde memory (Ref. s), removals of the perirhinal cortex (plus entorhinal cortex) have a temporally extensive effect (Ref. t). Consistent with these findings, clinical studies have shown that damage extending beyond the hippocampus into temporal cortical regions including perirhinal cortex can result in a temporally extensive and ungraded retrograde amnesia (Ref. u).

Yet another challenge for the unitary system view derives from recent reports suggesting that damage to the hippocampus yields severe deficits in episodic memory, but largely spares semantic memory. For example, a recent case report of an adult amnesic patient demonstrates efficient acquisition of semantic knowledge in the absence of acquisition of episodic memory (Ref. v). Similarly, young patients who received damage to the hippocampus in childhood exhibit poor episodic memory while at the same time are competent in basic academic abilities such as reading, writing, and arithmetic (Ref. w). (It should be noted, however, that spared episodic memory might be able to support, over time, the acquisition of semantic memory. The extent to which episodic memory might support semantic memory in these young subjects is presently unclear.) Taken together, these findings argue against the idea that the medial temporal lobe structures operate together as a single functional unit.

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perirhinal cortex participates in memory in at least three ways: acquisition, retrieval, and long-term storage. Evidence from the ablation and physiological studies reviewed in this article suggests a critical role for the primate perirhinal cortex in the formation and retrieval of both intramodal and crossmodal stimulus–stimulus associations, associations that presumably endow objects with meaning. The perirhinal cortex, together with many other cortical fields, also serves as the site of long-term storage of such knowledge. Thus, perirhinal cortex, together with other brain regions, comprises a semantic network representing objects and object-related information, including words. It is critical for

Outstanding questions

- In humans, what are the functional specializations of the many ventromedial temporal cortical areas, and what are their anatomical relationships with the perirhinal cortex?
- What are the functionally equivalent temporal cortical areas in monkeys and humans?
- Can the cognitive deficits seen in patients with semantic dementia, such as those with Alzheimer's disease, be accounted for by the model we have described?
- How do area TE and perirhinal cortex interact with different subdivisions of the prefrontal cortex in perception and memory? And what other top-down influences affect information processing in the perirhinal cortex?
- What are the functions of the direct dopaminergic inputs that innervate the perirhinal cortex but not area TE? Can this provide a clue as to the functional specializations of perirhinal cortex as opposed to other regions of inferior temporal cortex?

many semantic (associative) processes, we submit, not because of any special computational function it might possess, but rather by virtue of its pivotal anatomical position, which allows the linking of representations stored in diverse sensory and motor areas.

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Oscillatory gamma activity in humans and its role in object representation

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We experience objects as whole, complete entities irrespective of whether they are perceived by our sensory systems or are recalled from memory. However, it is also known that many of the properties of objects are encoded and processed in different areas of the brain. How then, do coherent representations emerge? One theory suggests that rhythmic synchronization of neural discharges in the gamma band (around 40 Hz) may provide the necessary spatial and temporal links that bind together the processing in different brain areas to build a coherent percept. In this article we propose that this mechanism could also be used more generally for the construction of object representations that are driven by sensory input or internal, top-down processes. The review will focus on the literature on gamma oscillatory activities in humans and will describe the different types of gamma responses and how to analyze them. Converging evidence that suggests that one particular type of gamma activity (induced gamma activity) is observed during the construction of an object representation will be discussed.

Whhen one searches for a familiar person in a crowd, different cues (height, face, clothes, etc.) are retrieved from memory and combined to form a coherent representation of the desired person. Similar representations are used in many situations and can be composed of many different features and include visual, auditory, semantic, or even emotional information. Data from numerous neuropsychological and neuroimaging studies in humans[1,2], and neurophysiological studies in animals[3], indicate that the processing of these different features involves anatomically distinct

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