The Parahippocampal Region: Corticocortical Connectivity

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ABSTRACT: The parahippocampal region, as defined in this review, comprises the cortical regions that surround the rodent hippocampus including the perirhinal, postrhinal, and entorhinal cortices. The comparable regions in the primate brain are the perirhinal, parahippocampal, and entorhinal cortices. The perirhinal and postrhinal/parahippocampal cortices provide the major poly-sensory input to the hippocampus through their entorhinal connections and are the recipients of differing combinations of sensory information. The differences in the perirhinal and postrhinal cortical afferentation have important functional implications, in part, because these two regions project with different terminal patterns to the entorhinal cortex. The perirhinal cortex projects preferentially to the lateral entorhinal area (LEA), and the postrhinal cortex projects preferentially to the medial entorhinal area (MEA) and the caudal portion of LEA. Although the perirhinal and postrhinal cortices provide the major cortical input to the entorhinal cortex, the entorhinal cortex itself receives some direct cortical input. An examination of the cortical afferentation of the entorhinal cortex reveals an interesting principle of connectivity among these regions; the composition of the direct neocortical input to the LEA is more similar to that of the perirhinal cortex, and the composition of the direct neocortical input to the MEA is more similar to that of the postrhinal cortex. Thus, polymodal associational input to the LEA and the MEA exhibits some segregation and is organized in parallel. The organization of intrinsic connections for each of the parahippocampal regions also contributes to the segregation of information into parallel pathways.

INTRODUCTION

The parahippocampal region comprises a group of cytoarchitectonically and connectionally distinct cortical regions. While these regions are easily discriminable, what joins them is that together they account for the large majority of the cortical input to the hippocampus. In this chapter. I briefly review the fundamental neuroanatomical features of the perirhinal. postrhinal, and entorhinal cortices, the cortical afferentation of these regions, and rhc organization of the interconnections among these regions in the rat brain. Along the way comparisons will he made with what is known about the mouse, monkey, and human bruins.

Studies in the human, monkey and rat now suggest that the parahippocampal regions contribute substantially to sonic memory processes.[1-5] The suspected role of these regions in normal memory function initiated a flurry of neuroanatomical stud-

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ies conducted primarily in the monkey and the rat.[6-17] For some years now we have known that the the majority of the cortical input to the hippocampus is funneled through the association cortices that surround the hippocampus. Neuroanatomical approaches show that the individual areas within the parahippocampal region differ in their structural and connectional organization, suggesting that they are not merely conduits of information for the hippocampus, but that they have different functions with regard to memory. This notion of differential contributions is supported by differences among them in cortical and subcortical afferentation, patterns of intrinsic connectivity, and patterns of interconnectivity.

The large majority of research on hippocampal and parahippocampal function has been conducted in rat and monkey models. Consequentially, an important question is the extent of neuroanatomical and functional homology with similar regions in the human brain. The recent increase in the use of mutant mice to study hippocampal function also raises questions of how the parahippocampal regions in the mouse compare with the comparable regions in the rat, monkey and human brains. Although considerable information is now available about the structure and function of parahippocampal regions in the rat and monkey brains, the data on the these regions are lacking for the mouse and human brains. It will be important to document cross-species differences in these regions to promote the usefulness of animal models of human memory.

NOMENCLATURE

In the rodent brain, there is a prominent sulcus, the rhinal sulcus, that arises at the joining of the olfactory bulb and frontal pole and extends almost to the caudal pole of the brain (FIG. 1). The caudal extension of the rhinal sulcus in most rats is barely evident as no more than a shallow indentation. The cortical regions that surround the caudal portion of the rhinal sulcus in the rat brain include the perirhinal, postrhinal, and entorhinal regions. In the primate brain, the three comparable regions are the perirhinal, parahippocampal, and entorhinal cortices. Although still identifiable, the rhinal sulcus is substantially more limited in extent in the monkey and is even less prominent in the human brain (FIG. 2). In the primate brain, then, only the perirhinal and entorhinal (rhinal cortices) are contiguous with the rhinal fissure. In both the rodent and the primate brains. the three regions can be described as surrounding the hippocampus; thus, the term "parahippocampal region" is especially useful in a comparative framework. Nevertheless, care must be taken not to equate the term with "parahippocampal cortex" or "parahippocampal gyrus" in the primate brain.

In the rat, the perirhinal cortex consists of areas 35 and 36 (reviewed in Ref. 3). The postrhinal cortex has not been subdivided at this writing. In the monkey, the perirhinal cortex consists of areas 35 and 36, and area 36 is further partitioned into five subdivisions. The monkey parahippocampal cortex consists of areas TH and TF, each comprising two subdivisions.[16] Although the data on the mouse and human are sufficiently limited as to preclude a confident application of a consistent nomenclature across species, indications are that the regions that surround the hippocampus can at least be divided into three comparable regions: perirhinal, postrhinal, and entorhinal for the mouse (FIG. 1A); perirhinal, parahippocampal, and entorhinal for the human (FIG. 2B).
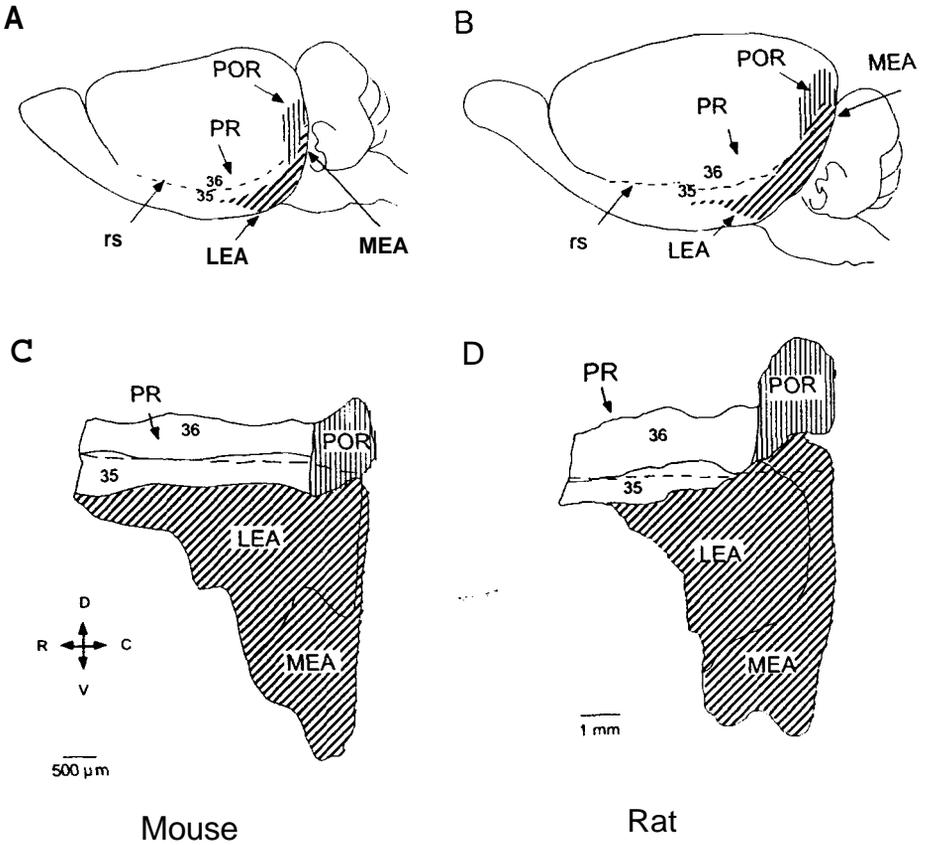
FIGURE 1. A lateral surface view of the mouse brain (A) and the rat brain (B; adapted from Burwell et al.[3]). Unfolded two-dimensional surface maps of the mouse (C) and the rat (D) entorhinal, perirhinal and postrhinal cortices. Perirhinal cortex (PR, areas 35 and 36) is shown in gray, postrhinal cortex (POR) in vertical stripes, and the entorhinal cortex (EC) in diagonal stripes. LEA, lateral entorhinal area; MEA, medial entorhinal area.

The perirhinal cortex exhibits substantial cross-species similarity in cytoarchitectonic features in the rat and monkey brains (see below), but the postrhinal and para-hippocampal regions share few apparent structural or cytoarchitectonic similarities. Thus, in defining these areas in the rat brain, Burwell and colleagues[3,18] called the region postrhinal cortex, a name already found in the rodent literature,[19] rather than employing terminology in use for the primate brain. Subsequent connectional studies indicated that the rat postrhinal and monkey parahippocampal regions exhibit striking connectional similarities,[9,15] which provided the basis for hypothesizing functional homology between the two regions.
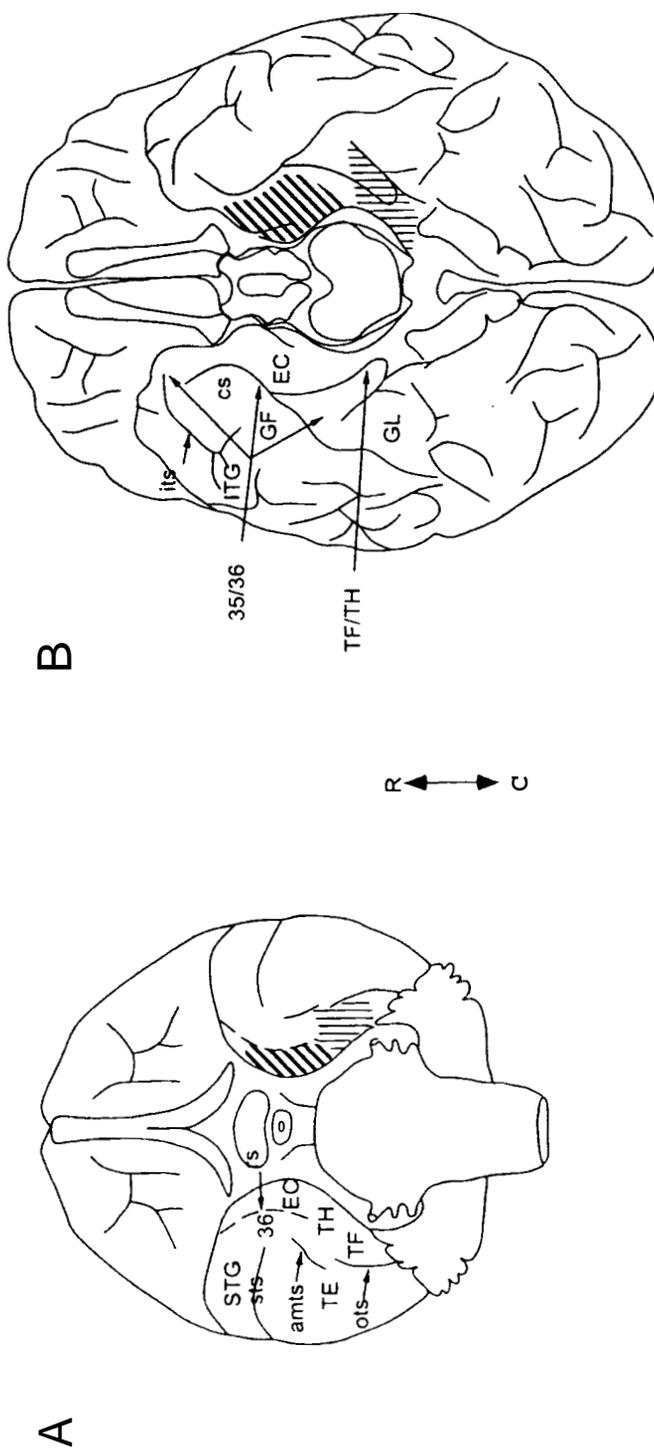
FIGURE 2. Ventral surface views of the monkey brain (A; adapted from Suzuki & Amaral[16]) and the human brain (B; adapted from Insausti, Tuñón, et al.[46]) showing borders of the entorhinal (EC), perirhinal (PR), and parahippocampal (PH) cortices as described in this chapter. amts, anterior middle temporal sulcus; Audv, auditory association cortex; cs, collateral sulcus; GF, fusiform gyrus; GL, lingual gyrus; ITG, inferotemporal gyrus; its, inferotemporal sulcus; Is, lateral sulcus; ots, occipitotemporal sulcus; PaSub, parasubiculum; rs, rhinal sulcus; STG, superior temporal gyrus; area TE of von Bonin and Bailey (1947); and Visl, visual association cortex.
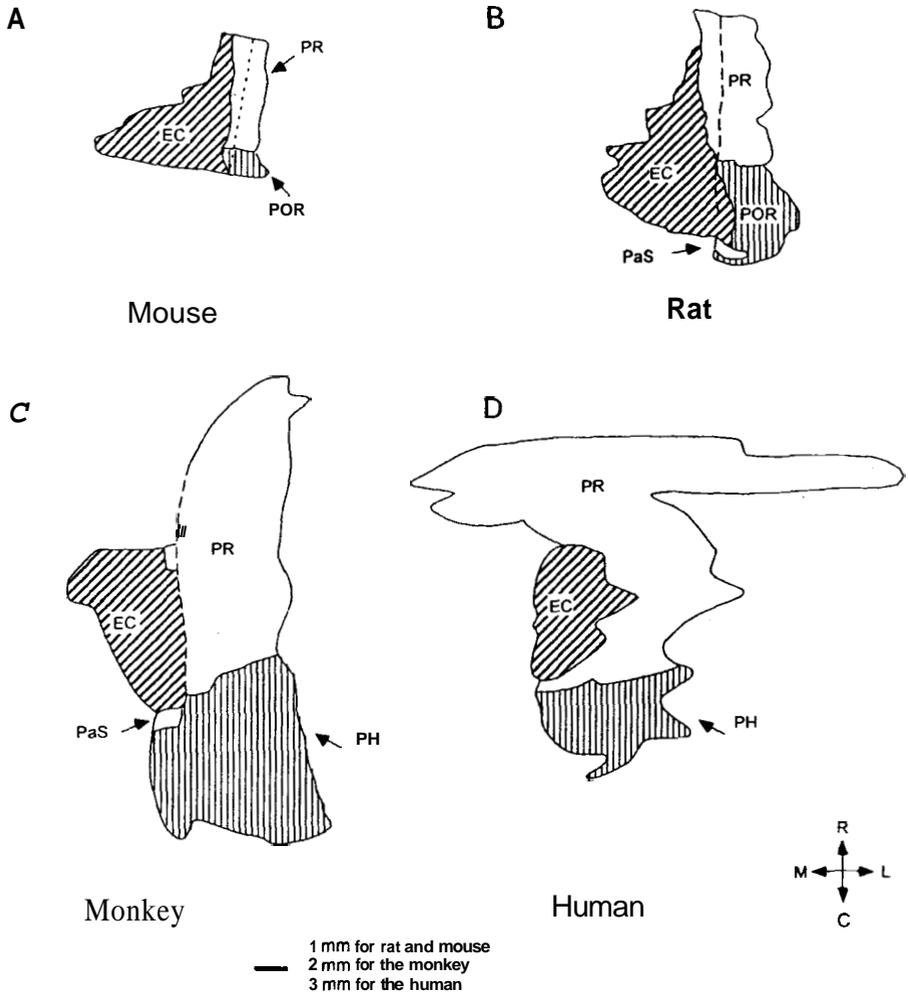
FIGURE 3. Representative unfolded two-dimensional maps. For comparison, unfolded maps for all four species are shown here. Either layer IV or a line between layers III and V was unfolded in the mouse (A) and rat (B), layer IV was unfolded in the monkey **(C),** and the outer margin of layer V was unfolded in the human (D). Again, perirhinal cortex (areas 35 and 36) is shown in gray, parahippocampal (PH) and postrhinal (POR)cortices in vertical stripes, and the entorhinal cortex (EC) in diagonal stripes. PaSub, parasubiculum.

STRUCTURE AND CYTOARCHITECTONIC FEATURES

Unfolded maps of layer IV of the parahippocampal region of four species (FIG. 3, note the differences in scale) provide the basis for some interesting comparisons. Allowing for differences in size and shape, the spatial relationships among the sub-areas are similar in the mouse, rat, monkey, and human brains. Although there are obvious differences in absolute size, the perirhinal cortex accounts for about 5% of the total cortical surface area, at least for the rat and monkey.[3,20] Thus, it has been
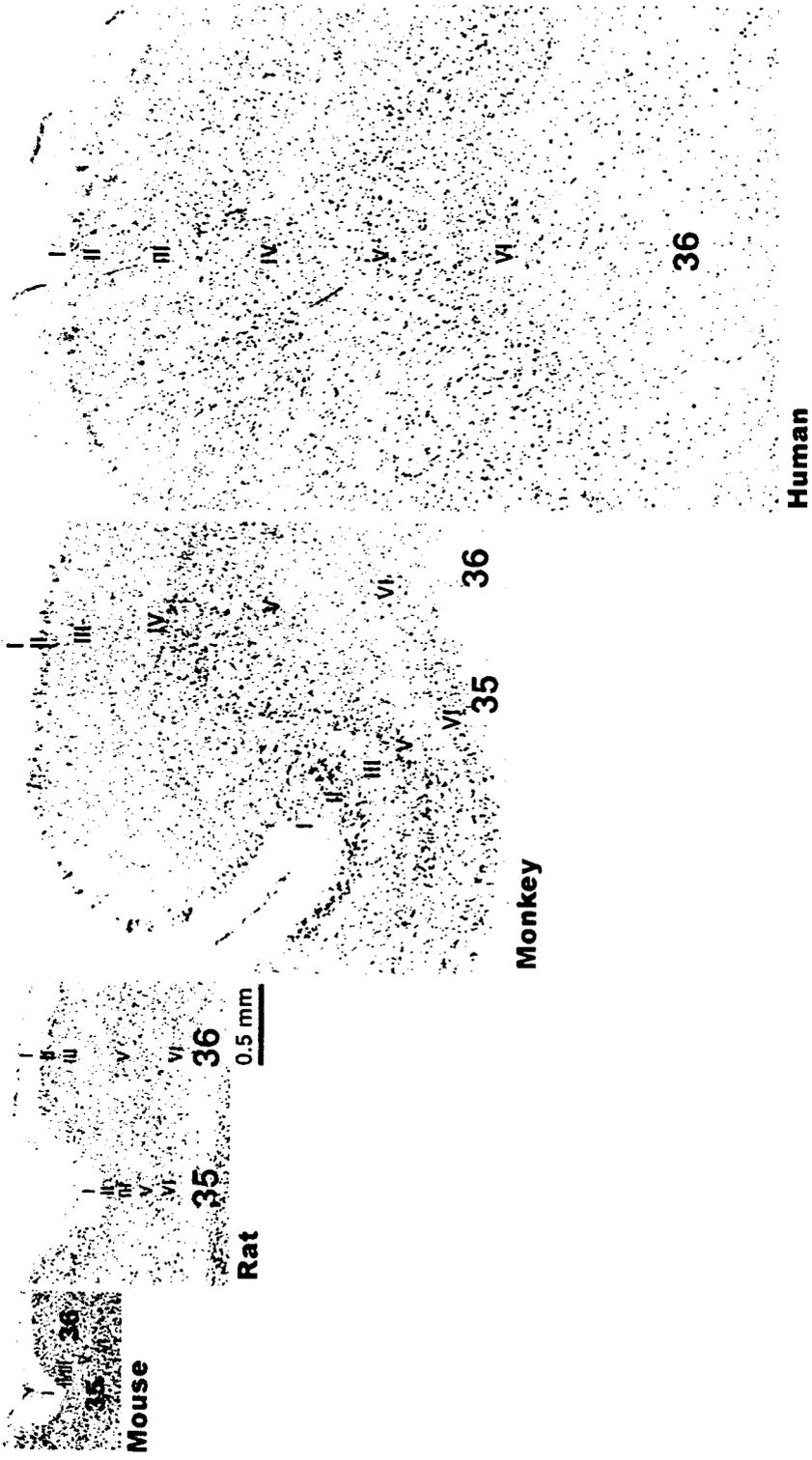
FIGURE 4. Photomicrographs of Nissl-stained coronal sections through perirhinal cortex (areas 35 and 36) of the mouse (**A**), rat (**B**), the macaque monkey (**C**), and the human (**D**). The laminar pattern is indicated by Roman numerals. Note that the characteristic patchy layer II is apparent in all four species.

TABLE 1. Cortical surface area (sq mm)

Region	Mouse	Rat	Monkey	Human
Perirhinal cortex	1.50	9	93 .	422
Parahippocampal or postrhinal cortex	0.36	5	78	89
Entorhinal cortex	3.50	12	**41**	81

SOURCE: Burwell et *al.*[45] for areas for rat, monkey, and human; Burwell, unpublished observations, for areas for the mouse.

suggested that the perirhinal cortex may scale up relative to cortical surface area. It is noteworthy that the relative sizes of the other cortices vary across the four species (TABLE 1). For example, the size of the entorhinal cortex appears to scale down exponentially with increase in cortical surface area, suggesting that the area might be less important as one goes up the evolutionary scale.

In addition to cortical surface area, another cross-species difference is apparent in cortical thickness. FIGURE 4 shows the perirhinal cortex of the mouse, the rat, the macaque monkey, and the human brains in coronal section in the same scale. This cortex is substantially thicker in primate brains as compared with the rodent models. Additionally, the laminar characteristics of the cortex are much more prominent in the primate brains as compared to either rodent model. Yet, as we shall see, closer comparisons indicate that there are similarities in the general organizational principles of the perirhinal and parahippocampal/postrhinal cortices across species as well as some signature characteristics that are common across species.

All reports of the cytoarchitecture of area **35** of the rat perirhinal cortex indicate that the region is **agranular**.[3,21,22] Recent investigations further conclude that it is distinguished by a prominent layer V characterized by large, darkly staining pyramidal **cells**.[3] Area **36** is easily distinguished cytoarchitectonically from area **35** because it is granular. Additionally, area **36** has a distinctive layer II characterized by patches of spherical and pyramidal cells. In the ventral subdivision, only a weak layer IV is present such that the granule cells are intermixed with the cells forming layers III and V. This granular layer is more distinct at progressively more dorsally situated portions of area **36.**

The available cytoarchitectonic information on the perirhinal and postrhinal cortices in the rat indicates that there are similarities with the monkey. The macaque monkey area **35** is agranular and homogeneous in its cytoarchitectonic characteristics as is true for the **rat**.[4,15,23,24] Layer V is populated by large, darkly staining, densely packed cells. **As** in the rat, these cells form an arc around the fundus of the rhinal sulcus. In contrast to area **35,** area **36** shows substantial cytoarchitectonic regional variation. In general, it becomes more densely cellular, more columnar, and more distinctly laminated as one moves either laterally or caudally.[15] Unlike area **35,** area **36** has a distinct layer IV, although it tends to be very weakly populated in the medial and rostral portions of the area. In the monkey as in the rat, the most distinctive feature of area **36** is the patchy layer II, which is composed of islands of darkly stained cells that form an irregular border with layer I, especially at rostral levels. In fact, this characteristic patchiness of area **36** layer II is easily identified across species in the mouse, rat, monkey, and human (FIG. **4).**

The postrhinal cortex in the rat is not clearly differentiated from the perirhinal cortex on cytoarchitectonic grounds. This may be in part because of the way in which postrhinal cortex wraps obliquely around the caudal pole of the rat brain. This spatial arrangement makes it impossible to clearly observe the organization of laminar and cellular characteristics without dissecting out the region and flattening it. Thus, in most planes of the section, the border between the rat perirhinal and postrhinal cortices is difficult to ascertain. In coronal sections, the rostrally adjacent perirhinal cortex can be distinguished from the postrhinal cortex by the presence of ectopic layer II cells in the postrhinal ventral division. These outpouchings of cells into layer I give layer II a distinctively irregular appearance. In general, the postrhinal cortex is more highly laminated than perirhinal cortex, the cells are smaller and more homogeneously packed, and the cortex exhibits a weak granular layer. In the caudal half of the region, the lamination is obscured by the plane of sectioning.

In the monkey, the parahippocampal cortex comprising areas TH and TF is easily distinguished from the neighboring perirhinal region. The rostral portion of area TH is agranular and bilaminate in appearance due to the merging of layers II/III and layers V/VI. The caudal subdivision of area TH is more laminar in appearance and contains a meager internal granular layer. In contrast, area TF is more highly granular with large pyramidal cells populating a layer V that merges with layer VI.

CORTICAL AFFERENTATION

The perirhinal and postrhinal cortices of the rat receive widespread and entirely different neocortical input from unimodal and polymodal associational areas. Although earlier studies provided the initial information about perirhinal afferentation,[19,25–28] our recent more quantitative study based on new borders confirmed and extended the earlier findings (FIG. 5).[9] Perirhinal cortex receives a substantial olfactory input from piriform cortex (FIG. 5, upper left), which terminates almost exclusively in area 35. All other cortical input terminates preferentially in dorsal area 36 and is distributed across all remaining sensory modalities. The postrhinal cortex, in contrast, receives strong input from visual and visuospatial association cortex, somewhat less input from auditory association regions, and only weak input from the remaining modalities.

Our recent examination of the polymodal associational input to the perirhinal and postrhinal cortices (FIG. 5, lower)[9] confirmed, in a more quantitative manner, earlier reports of substantial associational input to perirhinal cortex.[19,28–31] Again, the two regions receive very different complements of cortical associational input. Projections from ventral temporal association cortices to the perirhinal cortex have been well-documented,[19,31,32] and we now know that the postrhinal cortex also receives ventral temporal input. The location of the origins of that input, however, differs for the two regions. The perirhinal cortex is interconnected with the full rostrocaudal extent of ventral temporal association cortex (Te, as defined by Swanson), whereas the postrhinal cortex is interconnected preferentially with the caudal portion of the region. Our earlier observations indicate that rostral Te, receives more input from somatosensory regions, mid-rostrocaudal portions from auditory regions, and the caudal portion from visual regions.' Thus, the organization of perirhinal and postrhi-
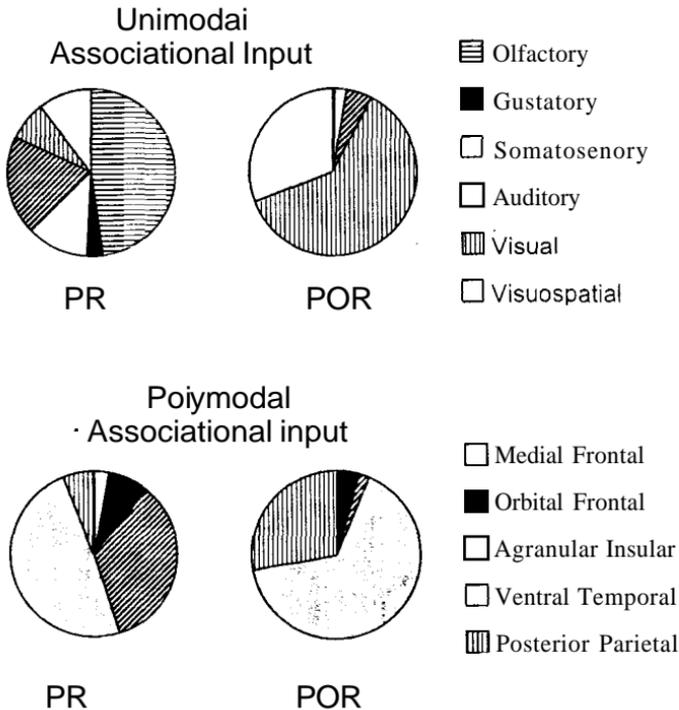
Unimodal Associational Input

- ⊞ Olfactory
- ■ Gustatory
- ☐ Somatosenory
- ☐ Auditory
- ▥ Visual
- ☐ Visuospatial

PR   POR

Poiymodal · Associational input

- ☐ Medial Frontal
- ■ Orbital Frontal
- ☐ Agranular Insular
- ☐ Ventral Temporal
- ▥ Posterior Parietal

PR   POR

FIGURE 5. Pie charts showing the proportion of unimodal associational input to the perirhinal cortex (PR, *upper left*) and the postrhinal cortex (POR, *upper right)*. Pie charts showing the proportion of polymodal associational input to the perirhinal cortex (PR, *lower left),* and the postrhinal cortex (POR, *lower right)*. Ventral temporal cortex here represents a band **of** cortex that lies along the dorsal borders of the perirhinal and postrhinal cortices. **The** perirhinal cortex receives input from more rostral portions of this region, whereas the postrhinal cortex receives input from more caudal portions of this region.

nal input from ventral temporal areas further upholds the principle that the perirhinal cortex receives input from all sensory modalities, whereas postrhinal cortex is preferentially innervated **by** visual and visuospatial regions.

Although the perirhinal and postrhinal cortices receive substantially more input from higher-order polymodal associational regions, the entorhinal cortex does itself receive some extra-peri-postrhinal associational input **(FIG. 6).** Interestingly, the direct associational input to the lateral entorhinal area **(LEA)** is more similar to that of the perirhinal cortex in that it arises predominantly in anterior associational regions such as medial frontal cortex. The medial entorhinal area (MEA), in contrast, receives direct associational input more similar to that of the postrhinal cortex in that it arises predominantly in posterior associational regions such as retrosplenial cortex.

The perirhinal and parahippocampal cortices of the macaque monkey are also distinguished by their cortical input.[15,24,33,34] Suzuki and Amaral[15] provided evidence that unimodal associational inputs arise from somatosensory, auditory, and visual as-
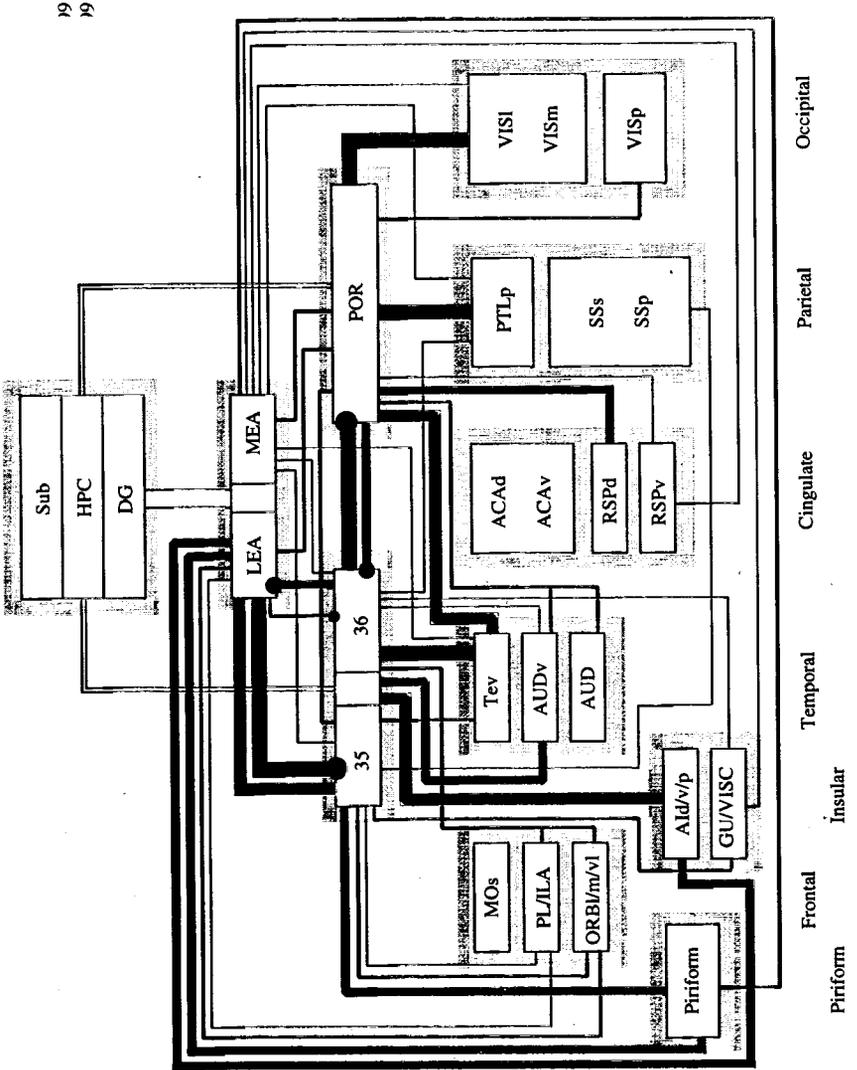
FIGURE 6. *See following page for caption.*

sociation cortices. Different from the rat, the majority of the input to both of these cortices is from visual areas although not the same visual regions. Visual object information derived from projections originating in area TE predominantly reaches the perirhinal cortex, whereas visuospatial information, arising from posterior parietal cortex and area V4, is more heavily directed to the parahippocampal cortex. Cortices identified with somatosensory processing, primarily the granular and dysgranular insular cortices, project both to perirhinal and parahippocampal cortices. Unlike the rat in which auditory association cortex projects to both perirhinal and postrhinal cortices, in the monkey only the parahippocampal cortex receives input from auditory associational regions. The monkey perirhinal and parahippocampal cortices receive polysensory information from ventrolateral and orbital cortices, cingulate and retrosplenial cortices, posterior parietal cortex, and the polymodal region of the dorsal bank of the superior temporal sulcus.[15] All of these cortices project to parahippocampal cortex, but the predominant polymodal associational input to perirhinal cortex arises from the parahippocampal cortex and the superior temporal sulcus. Interestingly, in both the rat and the monkey, the parahippocampal/postrhinal cortex projects heavily to the perirhinal cortex, whereas the reciprocal projection is relatively meager.

INTRINSIC CONNECTIONS

We previously identified a number of principles of intrinsic connectivity in the parahippocampal region.[7] Area **36** of the perirhinal cortex has extensive intrinsic connections such that any location is connected to the entire subregion (FIG. 7A). The projections are heaviest to the locations closest to the origin and attenuate as the distance from the origin increases. Although projections to a focus in area **36** originate about equally from regions located rostrally and caudally fo the focus, there is a prominent dorsal to ventral gradient. This dorsal to ventral polarity is also reflected in connections between areas **35** and **36.** Continuing the dorsal to ventral polarity of projections, area **36** projects heavily to area 35, but area **35** returns a weaker projection to area **36.** In general, the ventrally directed projections terminate at the same rostrocaudal level at which they originate. The area **36** projection to area **35** resembles a lateral pathway according to criteria described by Felleman and Van Essen;[20] that is, the cells in superficial and deep layers terminate in all layers. In contrast, the

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FIGURE 6. A diagram representing the pattern and strength of the cortical connectivity of the hippocampal formation [dentate gyrus (DG), hippocampus proper (HPC), subicular complex (sub), and entorhinal cortex **(EC)]**, the perirhinal cortex (PR, areas 35 and 36), and the parahippocampal (PH, areas TF and TH) or postrhinal cortices (POR) for the rat. The thickness of the **solid fines** represents the relative strength of the remaining cortical input to the respective areas based on densities of labeled neurons. **Open lines** reflect connections that are known, but were not quantified in the referenced study. **ACA,** anterior cingulate cortex; AId, v, and p, dorsal, ventral, and agranular insular cortices; Aud, primary auditory cortex; AUDv, auditory association cortex; GU, gustatory granular insular cortex; MOp and MOs, primary and secondary motor areas; Pir, piriform cortex; RSP, retrosplenial cortex; SSp and SSs, primary and supplementary somatosensory areas; VISC, visceral granular insular cortex; VISl and m, visual association cortex; VISp, primary visual cortex.
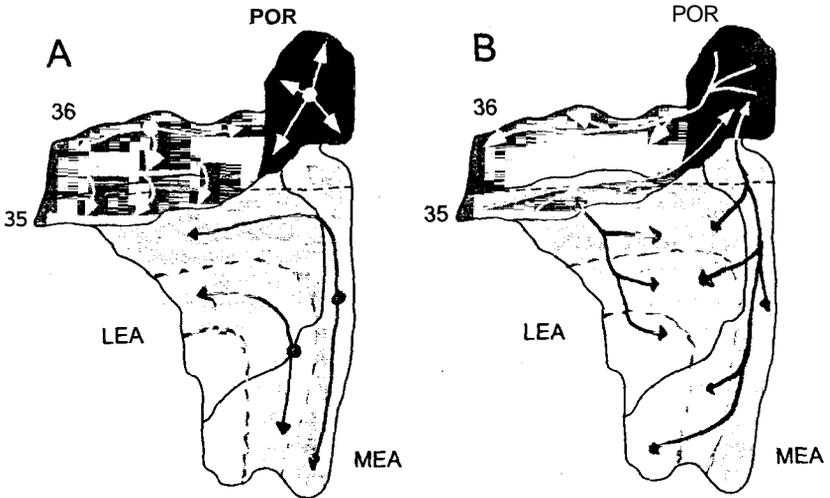
FIGURE 7. Unfolded maps of the parahippocampal areas in the rat showing the patterns of intrinsic connections (left) and the patterns of interconnections (right). The postrhinal cortex (POR) is shown in dark grey, the perirhinal cortex (PR) in middle grey, and the entorhinal cortex (EC) in three shades of light grey. The shades of light grey for the entorhinal cortex are progressively lighter to represent the lateral to medially located dentate-gyrus projecting bands. See text for details.

return projection exhibits characteristics of a feedback pathway in that the projection exhibits a bilaminate origin in area **35** and a bilaminate termination in area **36.**

Unlike area **36** and area **35,** the intrinsic connections of POR exhibit no polarity. Although they show **no** topography of terminations, the associational projections within POR are extensive. Thus, any focus within the region gives rise to strong intrinsic projections to the entire region (FIG. 7A). Indeed, this characteristic of the intrinsic connections of the postrhinal cortex was useful in defining its borders.[7] The laminar pattern of the postrhinal associational connections in the postrhinal cortex is similar to that found in area 36 in that they originate in layers II, V, and VI and terminate in layers I and V NI.

The entorhinal cortex exhibits an unusual organization of interconnections that does not respect cytoarchitectonically defined subfields. There are three lateral to medially located, nonoverlapping domains or bands, each of which contains portions of LEA and MEA (FIG. 7A). The associational projections terminate preferentially within the band of origin.[23,37–39] The intrinsic entorhinal connections arise in layers II and III and the deep layers, but terminate preferentially in superficial layers.[39] Thus, it appears that the entorhinal cells of origin of the perforant pathway receive associational input **from** both deep and superficial layers. Each band projects to a different septotemporal level of the dentate gyrus, hippocampus, and subiculum.[14,23,35,36] More specifically, a caudolaterally situated band of entorhinal cortex projects to the septal half of the dentate gyrus; an intermediate band projects to the third quarter; and a medially situated band project to the fourth septotemporal border.
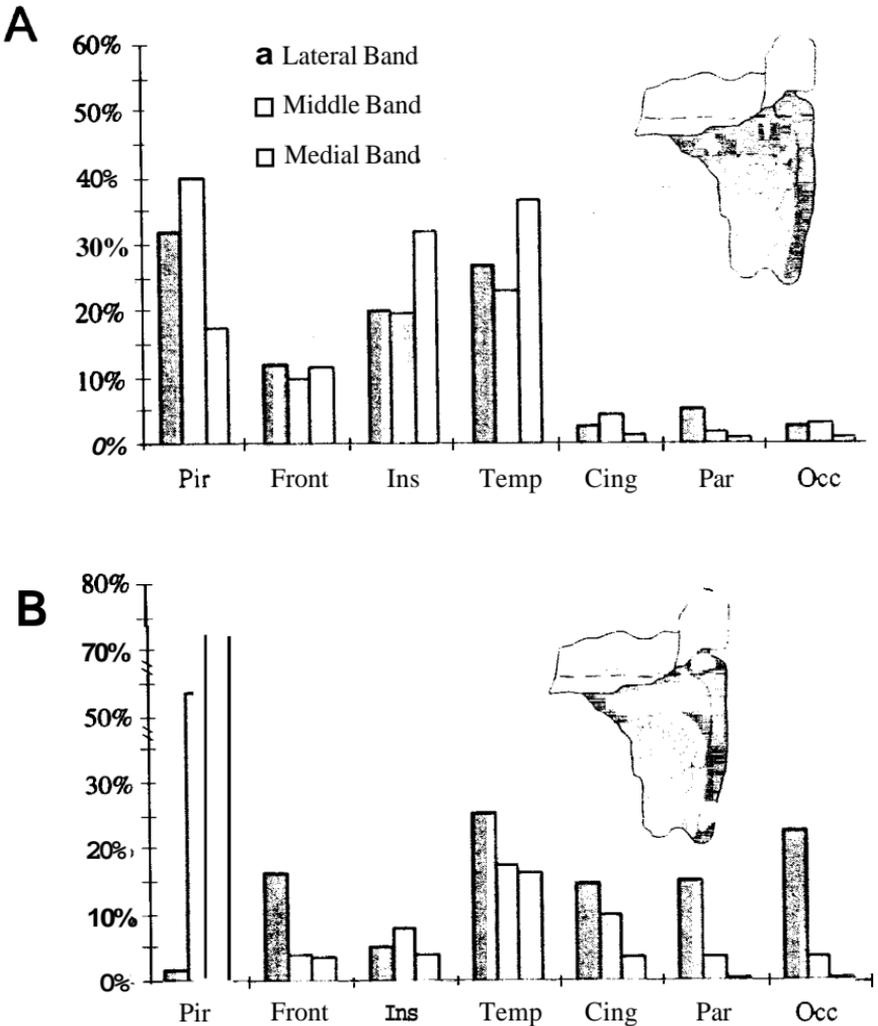
FIGURE 8. The results of a reanalysis of data from Burwell and Amaral[7] to show the organization of direct associational input **to** the entorhinal cortex according to its lateral to medially situated dentate-gyrus projecting bands. LEA, lateral entorhinal area; MEA, medial entorhinal area; perirhinal cortex areas 35 and 36; postrhinal cortex, POR.

The organization of entorhinal cortex into dentate-projecting bands appears also to reflect differences in cortical afferentation. Although the entorhinal cortex receives the majority of cortical input via the perirhinal and postrhinal cortices, it also receives some direct cortical input. We reanalyzed cortical afferent input to the entorhinal cortex' according to the medial to laterally situated bands and made some interesting discoveries. FIGURE 8 shows percentage of total input per band from different cortical regions for the LEA (panel A) and the MEA (panel B). Cortical input

appears to be ordered according to band, especially for the MEA. The lateral band, which would innervate septal levels of the dentate gyrus, receives the largest portion of polymodal association input that might be considered visuospatial in nature. In contrast, the middle and medial bands, which innervate more temporal levels of the dentate gyrus, receive the bulk of their input from olfactory regions. In fact, the MEA portion of the medial band is almost exclusively innervated by olfactory regions and thus shows some similarities in location and connectivity to the olfactory field of the monkey entorhinal cortex (EO).[40] It should be noted, however, that EO in the monkey is defined by olfactory bulb input and is considered to belong to the LEA.

INTERCONNECTIVITY

We now know that in the rat, as in the monkey, widespread cortical input reaches the hippocampal formation via the perirhinal and postrhinal cortices and their connections with the entorhinal cortex.[6,7,17,19] Thus, it is important to know how these two regions are interconnected in order to discern the influence each region has over hippocampal processing. The postrhinal cortex projects strongly to dorsal levels of the perirhinal cortex (FIG. 7B).[7] Accordingly, postrhinal input to the perirhinal cortex is likely to influence other cortical inputs that also terminate in dorsal levels of area *36.* The reciprocal projection — that from perirhinal cortex to the postrhinal cortex—is noticeably weaker and arises primarily from area 35.

The perirhinal and postrhinal cortices give rise to robust projections to the entorhinal cortex, which are stronger to the lateral band (**FIG.** 7B). Perirhinal cortex projects more strongly to the LEA and exhibits a topography such that rostral perirhinal cortex projects more strongly to rostral LEA, and caudal perirhinal cortex projects more strongly to caudal LEA. Postrhinal cortex projects preferentially to the **MEA** although it also projects to caudal LEA. Projections from the postrhinal cortex innervate all three DG-projecting bands of the entorhinal cortex, although the labeling in the lateral band is heavier. **As** in the monkey, the entorhinal cortex also gives rise to a return projection to the perirhinal and postrhinal cortices.[7,19,37,38] Moreover, the topography of the return projection is similar. The rostral entorhinal cortex (LEA) projects preferentially to the perirhinal cortex, whereas the caudal entorhinal cortex (caudal LEA and MEA) projects both to perirhinal and postrhinal cortices.

The topography of the entorhinal interconnections among the perirhinal, parahippocampal. and entorhinal cortices in the monkey was extensively described by Suzuki and Amaral.[16] Similar to the rat, the monkey parahippocampal cortex projects strongly to the perirhinal cortex, but the reciprocal projection is substantially weaker. Another similarity with the rat is that the perirhinal cortex projects most heavily to the rostrolateral two-thirds of the entorhinal cortex, and the parahippocampal cortex projects most heavily to the caudal two-thirds.

CONCLUSION

The intrinsic connections and interconnections of the parahippocampal areas are complex, but orderly in their arrangement. To summarize, the perirhinal and postrhinal receive different combinations of unimodal and polymodal sensory input. The
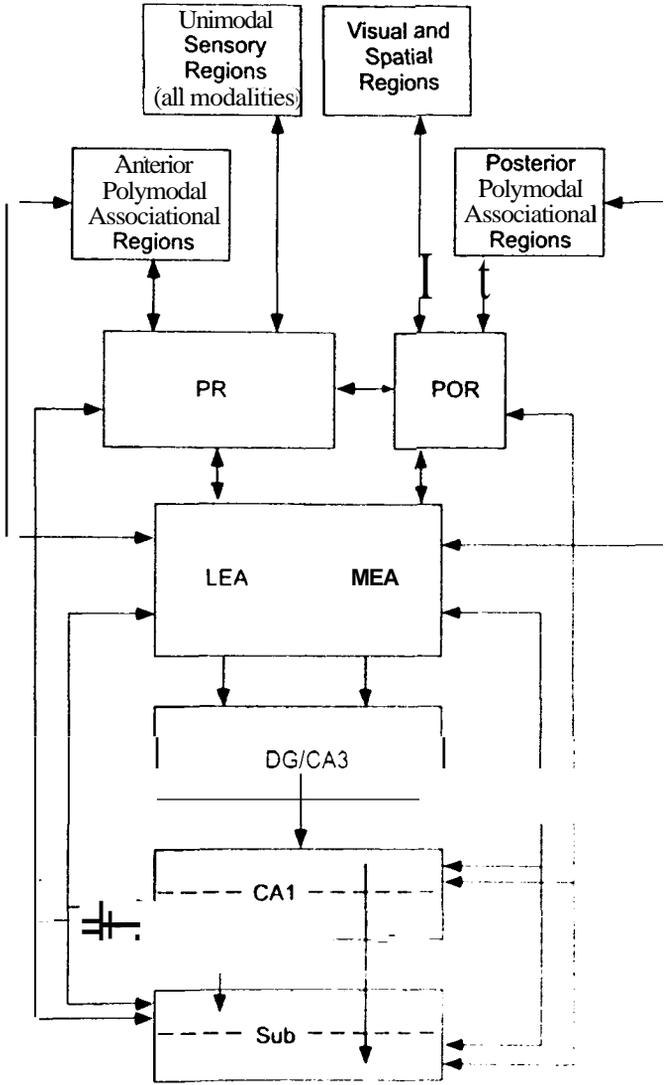
FIGURE 9. Schematic of corticohippocampal circuitry that shows the multiple parallel pathways by which unimodal and polymodal associational input reaches the hippocampal formation. Information appears to be somewhat segregated into a PR-LEA associated pathway (*light grey*), which is influenced by anterior associational regions such as the medial and orbital frontal cortices, and a POR-MEA associated pathway (*dark grey*), which is influenced by posterior associational regions such as the retrosplenial cortex. Several principles of connectivity are illustrated in the schematic. First, the polymodal associational input to PR vs. POR is similar to the direct polymodal associational input to the LEA and MEA, respectively. Second, PR and LEA project with similar terminal patterns to the CA1 field of the hippocampus and the subiculum; likewise POR and MEA terminate similarly in the CA1 and the subiculum. Third, there is convergence of information both in the dentate gyrus (DG) and CA3 field of the hippocampus, and in the intrinsic connections of the entorhinal cortex (see FIG. 7).

perirhinal cortex receives input from all modalites with the olfactory input terminating primarily in area **35** and all others terminating preferentially in dorsal area **36.** The postrhinal cortex is heavily innervated by visual and visuospatial regions. In terms of polymodal input, the perirhinal cortex tends to receive polymodal associational input from more anterior regions, whereas the postrhinal cortex **is** more closely interconnected with posterior polymodal associational regions. The exception is that perirhinal cortex does receive a strong input from the postrhinal cortex which also terminates in dorsal area 36. The perirhinal and postrhinal cortices project to different portions of the entorhinal cortex, maintaining some segregation **of** information flow. The flow of information is organized both according to cytoarchitectonic subdivisions (LEA and MEA) and according to the dentate-projection bands. Perirhinal cortex projects preferentially to LEA and postrhinal cortex projects preferentially to MEA and caudal LEA. The medial to laterally situated entorhinal bands are important in that they provide for both integration of information (within bands) and segregation of information (across bands), providing the circuitry for parallel pathways through the hippocampal formation. There is now evidence that a similar organization exists in the mouse entorhinal cortex[4'] and the monkey entorhinal cortex.[42] Thus, this feature of entorhinal connectivity appears to be conserved across species.

In conclusion, the perirhinal and postrhinal cortices in the rodent and primate brains are connected with both the full range of unimodal and polymodal associational cortices and with multiple fields of the hippocampal formation.[7,9,10,14–16] The organization of cortical afferentation, intrinsic connections, and interconnectivity suggests that there may be two parallel **corticohippocampal-processing** streams (**FIG.9**).

In neuroscientific research the parahippocampal region has been most consistently implicated in memory functions. Based on functional neuroanatomical grounds, however, it is reasonable to hypothesize an additional function for these regions in attention. The processing stream associated with the perirhinal cortex and anterior associational systems (**FIG.9**, light grey) includes prefrontal areas thought to contribute to attention and working memory. It is also interconnected with subcortical reward systems.[44] Based on the neuroanatomy, this stream might be involved in focused attentional processing of behaviorally relevant stimuli. In contrast, the processing stream more closely associated with the postrhinal cortex and posterior associational systems (**FIG.9**, dark grey) has robust connections with regions involved with visuospatial orienting, for example, the posterior parietal cortex and the lateral posterior nucleus of **the** thalamus. Thus, this processing stream is uniquely situated to contribute to attentional orienting toward spatially relevant stimuli. Continued investigation of these regions is necessary in order to fully understand their contributions to cognitive functions.

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