Neural connections of the posteromedial cortex in the macaque

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The posterior cingulate and the medial parietal cortices constitute an ensemble known as the posteromedial cortex (PMC), which consists of Brodmann areas 23, 29, 30, 31, and 7m. To understand the neural relationship of the PMC with the rest of the brain, we injected its component areas with four different anterograde and retrograde tracers in the cynomolgus monkey and found that all PMC areas are interconnected with each other and with the anterior cingulate, the mid-dorsolateral prefrontal, the lateral parietal cortices, and area TPO, as well as the thalamus, where projections from some of the PMC areas traverse in an uninterrupted bar-like manner, the dorsum of this structure from the posteriormost nuclei to its rostralmost tip. All PMC regions also receive projections from the claustrum and the basal forebrain and project to the caudate, the basis pontis, and the zona incerta. Moreover, the posterior cingulate areas are interconnected with the parahippocampal regions, whereas the medial parietal cortex projects only sparsely to the presubiculum. Although local interconnections and shared remote connections of all PMC components suggest a functional relationship among them, the distinct connections of each area with different neural structures suggests that distinct functional modules may be operating within the PMC. Our study provides a large-scale map of the PMC connections with the rest of the brain, which may serve as a useful tool for future studies of this cortical region and may contribute to elucidating its intriguing pattern of activity seen in recent functional imaging studies.

consciousness | default mode of brain function | emotion | posterior cingulate | precuneus

Recent functional imaging studies have shown an interesting pattern of activity in the posterior cingulate gyrus and the neighboring medial parietal cortex, an ensemble referred to as the posteromedial cortex (PMC). This region includes the posterior cingulate areas 23a, 23b, and 23c, the retrosplenial areas 29 and 30, the mesial parietal area 7m in the precuneus region, and area 31, which lies between the posterior cingulate area 23c and medial parietal area 7m (Fig. 1). The PMC shows deactivation during sleep (1) and propofol-induced anesthesia (2), and it is the first brain region to show an increased activity in patients regaining consciousness from persistent vegetative state (3). Moreover, the PMC is the most active brain area during a baseline state where normal subjects are asked to close their eyes and "rest" (4). In this condition, the PMC consumes ≈40% more glucose compared to the hemispheric mean (5). Of special relevance is the finding that the PMC (along with the lateral parietal and medial prefrontal cortices) routinely exhibits a decrease of activity during attention-demanding cognitive tasks unless they require a reference to the subject's notion of self (5, 6). For instance, when subjects think about how they would describe their own personality traits and physical appearance, the PMC shows increase of activity, but, in contrast, it shows deactivation when the same subjects make comparable judgments about a neutral reference person (7, 8). Although the role of PMC in emotions has been questioned (9), Maddock (10) found in a metaanalysis that the retrosplenial PMC is highly active when subjects retrieve autobiographical memories about emotional events in their life. In a study of our own, we found that the PMC is active when normal subjects reenact memories of happy events in their personal life (11).

The finding of similar activation pattern in imaging studies for the posterior cingulate and medial parietal regions raises the question of whether these two cortices serve some of the same functions and whether one can consider PMC to be a singular functional region. The behavioral and cognitive correlates of lesions confined to either the posterior cingulate or medial parietal cortices have not been studied in animals or patients with brain lesions. However, the few clinical observations in patients with such lesions suggest that consciousness is compromised in those patients (12).

Assuming that the function of a brain area is determined by the neural circuits to which it belongs, we reasoned that uncovering the neuroanatomical connections of the posterior cingulate and the medial parietal cortices would help us gain insight into their functional relationship with each other and with the rest of the brain.

We initiated the present study in the macaque because the cytoarchitectonic areas of the macaque posterior cingulate and medial parietal cortices resemble the ones in the human brain (13–16). In rodents, the posterior cingulate region is composed almost entirely of retrosplenial areas 29 and 30 with strong connections to the presubiculum, entorhinal cortex, and visual cortices (13). Like many other association cortices, the medial parietal cortex is not as developed in the rodent as it is in the primate brain (17).

It is already known that there are connections between some of the cytoarchitectonic areas of the macaque PMC and the anterior cingulate (15, 18–23), the prefrontal areas 9, 46 (24), and 11 (24, 25), the superior temporal sulcus and the parahippocampal region (15, 26, 27), the striatum (28), the thalamus (29, 30), and the basis pontis (31). Most of this evidence, however, is derived from studies in which the connections of structures other than the PMC were the primary focus of investigation, and different tracers with different sensitivities were used in different settings. Moreover, none of the past studies compared the pattern of connectivity of different PMC components with a given brain region, and none aimed at providing a comprehensive map of both subcortical and cortical, and of both afferent and efferent connections of *all* cytoarchitectonic areas within the PMC. Thus, a large-scale map of connectivity of the PMC remains unsketched. The present study is an attempt to overcome this gap of knowledge by using modern anterograde and retrograde tracers and analyzing the entire brain for PMC connectivity.

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Abbreviation: PMC, posteromedial cortex.

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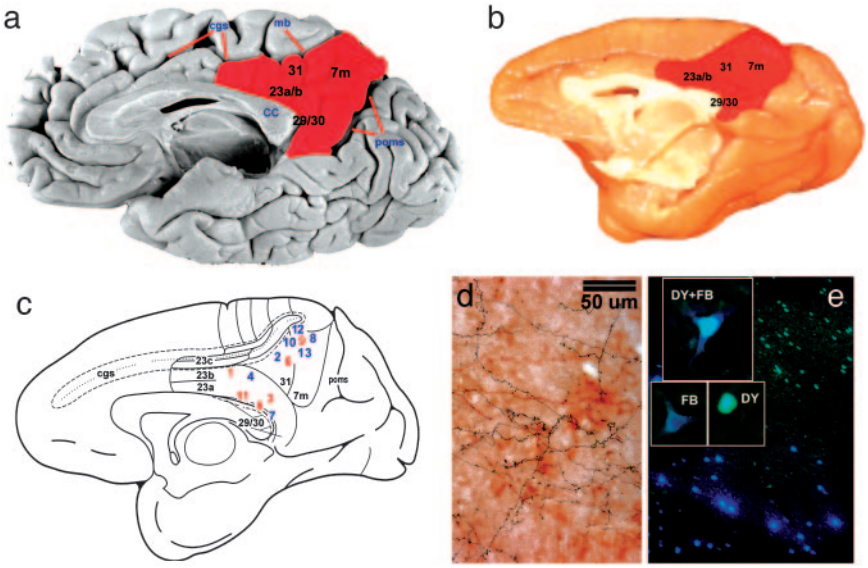

Fig. 1. Tracing the neural connections of the PMC. The PMC (highlighted in red in a and b) includes the posterior cingulate areas 23 a, b, and c, area 31, the retrosplenial areas 29 and 30, and the mesial parietal area 7m (i.e., the precuneus). These cortices are located dorsal to the corpus callosum (cc) and confined between the parietooccipital sulcus (poms), cingulate sulcus (cgs), and its marginal branch (mb). The macaque PMC (*b*) contains the same Brodmann areas and sulci (*c*). (*c*) The injection sites are shown in the anterograde (red) and retrograde (blue) experiments, respectively. Numbers correspond to the Exp column listed in Table 1. (*d*) The photomicrograph shows axonal terminals labeled for anterograde tracers, BDA (black) and FR (brown). The axonal varicosities or boutons are indicative of synaptic terminals, suggesting that these projections are not bypassing but terminal projections. (*e*) The photomicrograph is in a section of the brain visualized under fluorescent microscope showing cells that are labeled retrogradely with DY or FB or both (DY + FB).

Results

Our data analysis was based on the material in which the tracer injection was confined only to the cortical depth (Table 1), and we excluded cases with white matter involvement. Even with the injection of only 0.4–0.9 μl of tracer, we found that tracer material involved both 23a and 23b or both 29 and 30, and, for this reason, in the presentation of our data, these regions are referred to as 23a/b and 29/30, respectively. Connections mentioned in the text below are all ipsilateral unless specified otherwise. Details of our findings are presented in Figs. 2–5 (see also Figs. 6–11, Table 2, and *Results* in *Supporting Text*, which are published as supporting information on the PNAS web site).

Interconnections Among PMC Components. Our findings indicate that distinct cytoarchitectonic areas in the PMC are interconnected with each other, and the local connections are much denser between immediately adjacent areas than areas further apart. Moreover, neurons located within the same cytoarchitectonic boundaries are most densely connected (see *Supporting Text* for more details; see also Table 3, which is published as supporting information on the PNAS web site, for a list of abbreviations used in *Supporting Text*).

Connections with Other Brain Regions. ***Frontal lobe.*** The connections of the PMC with the frontal lobe involved mostly the mid-dorsolateral prefrontal cortex (mostly area 46d and 46v). All cytoarchitectonic areas within the PMC project to and receive projections from this prefrontal area, but the connectivity patterns are different for each PMC area (see *Results* in *Supporting Text* for more details). As an example, area 23b projects only to the ventral bank of principal sulcus in area 46v, whereas area 46d in the dorsal bank of the principal sulcus receives projections from area 23a.

Dorsal and dorsomedial parts of the frontal pole (areas 10d and

Table 1. Cases in this study

Experiments	Macaque	Case	Tracer	Site	Depth,* mm	Amount, μl
1	M150	M1-BDA-23B	BDA	23b	2.0	0.5
2		M1-FB-31	FB	31	1.5	0.8
3	IM152	M2-BDA-23a/b	BDA	23a/b	2.0	0.6
4		M2-FB-23a/b	FB	23a/b	3.3	0.5
5	IM153	M3-BDA-29/30(23a)	BDA	29/30(23a)	2.0	0.6
6		M3-FR-31	FR	31	2.0	0.7
7		M3-FB-30/23a	FB	30/23a	1.5	0.5
8		M3-DY-23a/b	DY	23a/b	2.0	0.7
9	IM154	M4-BDA-7m	BDA	7m	2.5	0.9
10	IM155	M5-FB-7m	FB	7m	2.5	0.6
11	IM156	M6-BDA-23a/30	BDA	23a/30	3.0	0.7
12	IM160	M7-FB-7m	FB	7m	2.0	0.7
13	IM162	M8-FB-7m	FB	7m	2.0	0.4

*Estimated depth at the time of surgery. BDA, Biotinylated Dextran Amine; FR, Fluoro-Ruby, DY, Diamidino Yellow; FB, Fast Blue.

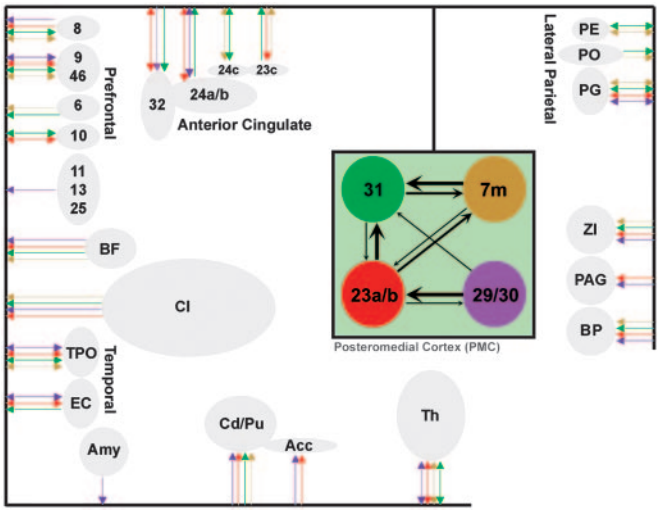

Fig. 2. Overview of the neural connections of the PMC. This cartoon illustrates that distinct areas of the PMC are interconnected with each other and share connections with some of the same brain structures. The interconnections among PMC components are not equally reciprocal. Note that the arrows within the green box have different thicknesses or some are absent. Colored arrows outside this box indicate connections between a specific PMC component and a given brain region. The direction of the arrows denotes whether a given brain region projects to or receives projection from a PMC component. For example, amygdala (Amy) only projects to the retrosplenial areas 29/30 but does not receive projections from it, whereas TPO is reciprocally interconnected with all of the PMC components. Acc, accumbens; Amy, amygdala; BF, basal forebrain; BP, basis pontis (relay to the cerebellum); Cd/Pu, caudate and putamen; CI, claustrum; EC, entorhinal cortex; PAG, periaquaductal gray matter; PE, superior parietal lobule; PG, posterior inferior parietal lobule; PO, opercular lateral parietal area; Th, thalamus; TPO, cortex buried in the superior temporal sulcus; ZI, zona incerta.

10dm, respectively) are reciprocally connected to areas 23a/b and 31, and, in a lesser extent, they send projections to 29/30. Other areas such as area 8, area 9, and 9/46 were also connected with the PMC, but the density of these connections was relatively low compared to area 46 connections with the PMC. Interestingly, the orbitofrontal and ventromedial prefrontal cortices were found to send projections to areas 29/30 only. Also, as shown in Figs. 9 and 10, we found that only areas 7m and 31 receive projections from the midlateral region of the premotor area 6.

Cingulate gyrus. Anterior cingulate areas 24a and 24b are interconnected with areas 23a/b and 29/30. Area 31 receives projections from these anterior cingulate areas, and area 7m targets only the anterior motor cingulate area 24c. Area 32 seems to receive projections mostly from area 23a and projects back to area 23b (see *Results* in *Supporting Text* for more details).

Parietal lobe. Area PG, which is the macaque equivalent for the human inferior parietal lobule, is reciprocally interconnected with all of the PMC areas. Area 31 receives dense projections from a widespread area within the PG (Fig. 9), whereas other PMC areas receive projections from only single foci within the PG (Figs. 7, 8, and 10).

The macaque equivalent for the human superior parietal lobule, area PE, parts of which serve as the supplementary somatosensory area, seems to be more interconnected with areas 31 and 7m. By comparison, area PO, or the lateral parietal cortex hidden within the intraparietal sulcus, sends projections to areas 31 and 7m.

Temporal lobe. Area TPO is located in the upper bank of the superior temporal sulcus and has at least three anterioposterior subdivisions. Of these subdivisions, we found that the most posterior subdivision is the one strongly interconnected with the PMC. Basolateral nucleus of the amygdala contained retrogradely labeled cells projecting to the retrosplenial areas 29/30 (Fig. 8). The entorhinal cortex, the pre- and parasubicular, and the subicular territories are also connected with the posterior cingulate areas, but area 7m only projects sparsely to the presubiculum (see *Results* in *Supporting Text* for more details).

Thalamus. All cytoarchitectonic areas in the PMC connect reciprocally with the dorsal-most sector of the thalamus. Notably, projections from areas 23a/b, 29/30, and 31 to the thalamus are continuous and aligned in a horizontal bar-like manner extending from the posterior to the anterior tip of the thalamus uninterruptedly traversing the nuclei anterior ventral (AV), anterior dorsal (AD), anterior medial (AM), superficial lateral dorsal (LD), dorsal tip of ventral lateral (VL) and ventral anterior (VA), lateral posterior (LP) and lateral pulvinar (Figs. 3 and 11). The nucleus reuniens receives projections only from areas 23a/b and 29/30 but not from areas 31 or 7m. In experiment 5, in which the anterograde tracer BDA involved areas 29/30, and, to a lesser extent 23a, projections cross the midline and innervate the contralateral anterior medial nucleus as well. In other words, the PMC innervates the anterior thalamus bilaterally in this case.

The pattern of thalamic projections back to the PMC is different from the corticothalamic pattern described above (Figs. 4 and 5). Areas 23a/b receive input from nuclei AV, AD, AM, LD, anterior intralaminar (aILN), LP, mediodorsal (pars MDdc), limitans, and pulvinar. Areas 29/30 receive afferents mostly from anterior and posterior nuclear groups, whereas area 7m receives its thalamic input primarily from the aILN, LP, and pulvinar and little, if any, from the anterior nuclear complex (Fig. 5). Area 31 is different from all PMC regions in that it receives projections from much more thalamic nuclei, i.e., the nuclei AV, AM, aILN, VL, MDdc, MDpc, LP, and anterior, lateral, and medial pulvinar. It is noteworthy that the number of neurons projecting to PMC was not equally distributed in all these nuclei. For instance, the number of neurons projecting to area 31 is almost 15-fold more in the posterior than the anterior thalamic nuclei. This ratio is almost inverse for projections to the retrosplenial PMC (Fig. 5).

Striatum. Projections from the PMC target several regions within the caudate nucleus. Although projections to the core regions of this nucleus are patchy and interrupted, the PMC projections to the dorsal domain of the nucleus are uninterrupted and continuous, spanning across the head and body of the entire nucleus before fading away gradually in its tail. The continuous bar of projections to the dorsal caudate region is a singular uninterrupted bar extending for $\approx$20,000 μm.

Several other points regarding the striatal projections of the PMC are noteworthy. First, there are contralateral projections to the caudate nucleus and the putamen, but these are noncontinuous and patchy. Second, the putamen is targeted relatively more by area 7m than other PMC areas. Third, different PMC areas target juxtaposing territories within the dorsal caudate nucleus (Fig. 11). Lastly, projections to the accumbens originate only in the retrosplenial areas 29/30 of the PMC.

Claustrum. The claustrum was found to be the source of strong projections to all of the PMC areas (Figs. 7–10). We observed that the number of claustrum cells projecting to any PMC region was relatively very high in every single case. On the other hand, the claustrum receives low density and patchy projections from areas 31 and 7m only.

Basal forebrain. The basal forebrain projections to the posteromedial cortex originate in the vertical and horizontal limb of the diagonal band of Broca. The cingulate areas receive projections from mostly the vertical limb of the diagonal band of Broca, whereas area 7m receives projections from the horizontal limb of the diagonal band of Broca and neighboring areas of the nucleus basalis of Meynert.

Basis pontis. Projections to the basis pontis (BP) were seen in every experiment and involved different territories of this region. For instance, projections from areas 23a/b were clustered in the rostral ventrolateral and caudal ventromedial domains of the BP (Fig. 11),

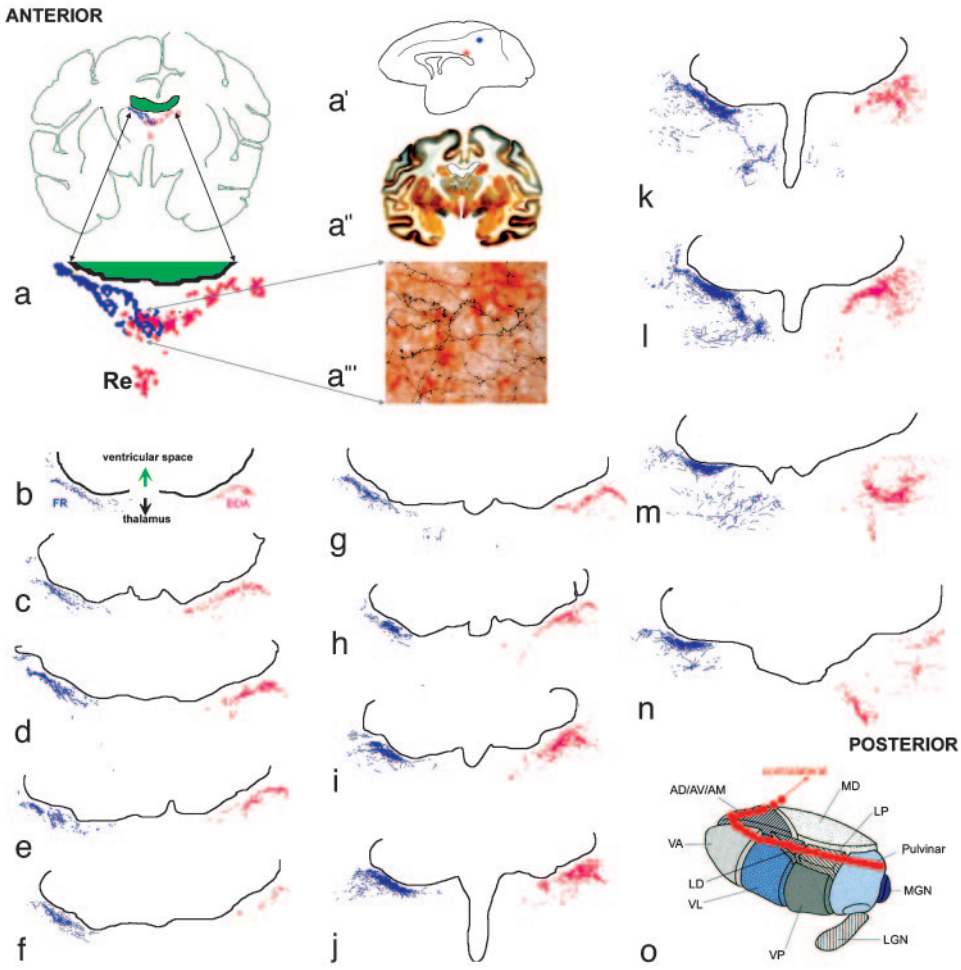

Fig. 3. Corticothalamic projections of the PMC. Fourteen consecutive coronal sections of the brain from anterior (*a*) to the posterior (*n*) levels of the thalamus show the anterograde corticothalamic projections from two different areas of the PMC in the same monkey (M3) by using the dual tracing method. Each section is 50-μm thick and 500 μm apart from the next. As shown in a′, areas 30/29 and a small segment of area 23a absorbed the injected anterograde tracer BDA (red), whereas area 31 in the contralateral side was injected with Fluoro-Ruby (blue). The black lines in *a*–*n* indicate the floor of the ventricle (the green highlighted space in *a*). (*a*″) A coronal section of the brain at the level of anterior thalamus processed with double immunohistochemistry by using antibodies against calbindin (light brown) and parvalbumin (dark blue). Terminal labeling in the nucleus reuniens (Re) is shown in *a*, and bilateral projections to the anterior medial thalamic nucleus are shown in *a* and pictured in *a*‴. Note how close the corticothalamic projections are to the floor of the ventricle. This approximity means that these projections target the dorsum (toward the top) of the thalamus. Also note how continuous these projections are. We have referred to this continuous pattern as the bar-like pattern of projections because they traverse the thalamic nuclei from the anterior most (*a*) to the posterior most (*n*) tip of the thalamus. (*o*) This drawing shows how the bar of corticothalamic projections traverses the dorsal nuclei of the thalamus in its entire extent and cross the midline in the anterior medial nucleus.

whereas area 7m targets the posterior and medial regions of the BP only.

Absent Connections. We found no direct connections between the PMC and primary sensory areas involved in the cortical representation of olfaction, internal milieu, the viscera, the body surface, audition, or vision. The sensory thalamic nuclei were also void of any connections with any of the PMC areas. Similarly, no direct connections with the primary motor cortex (area 4) were observed. Finally, we did not find projections from the monoaminergic nuclei of the brainstem reticular formation to the PMC.

Discussion

The possible merit of our study lies with providing a large-scale map of subcortical and cortical connections of all cytoarchitectonic areas within the PMC. Area 23c was not included in the present study because data about its connections were available from previous research, including the ones originated from our own laboratory (18, 19).

Our map is constructed in the macaque monkey, and our interpretations refer to the function of this brain region in the humans. We believe that this leap is justifiable. The macaque brain is the closest approximation to the human brain in conventional anatomical tracing experiments. Even though the functional role of the PMC in the macaque is largely unknown, the little data available suggest that this cortex might have similar, and perhaps, evolutionarily related functions in human and nonhuman primates. For instance, the cytoarchitectonic areas of the human PMC are well presented in the cynomolgus monkey (14–16), allowing for the possibility that the connectivity, and, thus, the function, of these same cytoarchitectonic areas might be similar in humans. Second, similar to its human counterpart, the PMC has the highest metabolic activity in the baseline resting state in the macaque brain (5) suggesting, at least partially, that the function of this brain region might be similar, if not identical, in the two brains.

The Neural Circuits of the PMC. All PMC components communicate with the anterior cingulate gyrus, mid-dorsolateral prefrontal cor-

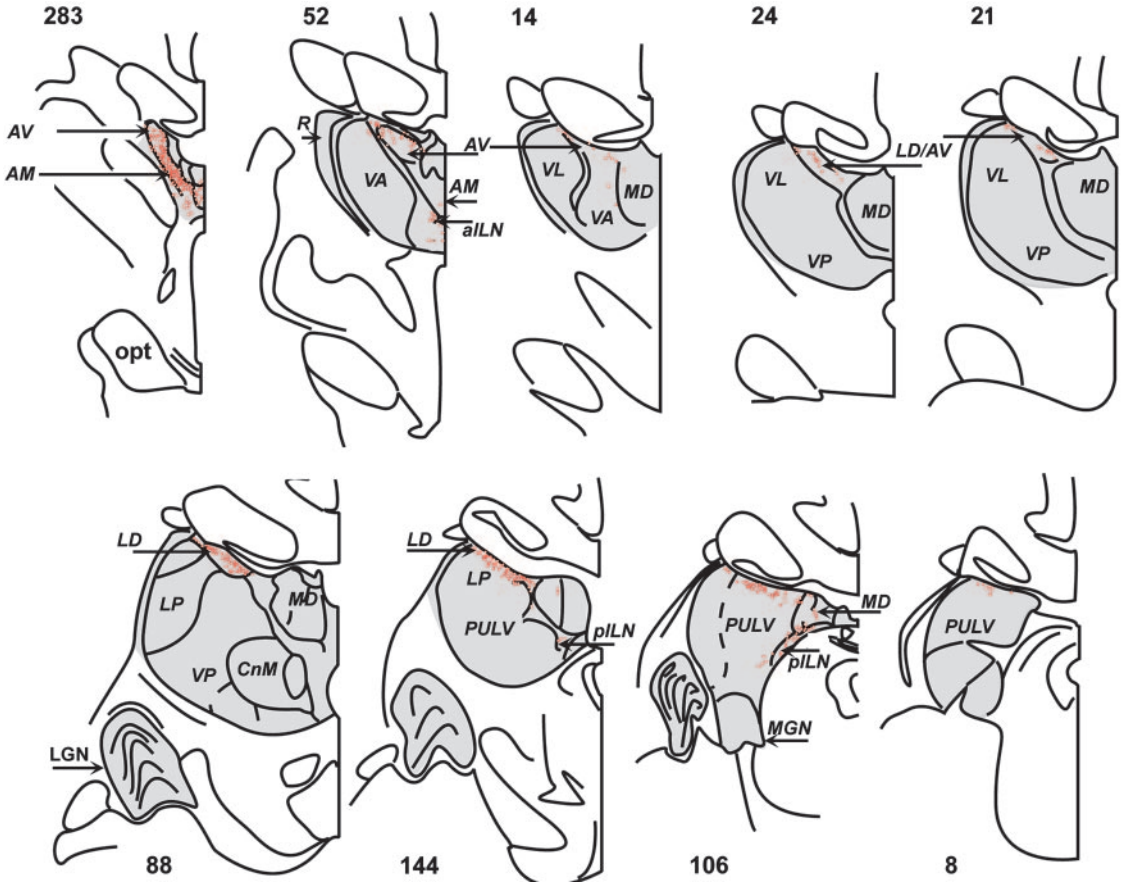

Fig. 4. Thalamocortical connections of the PMC. Red dots represent retrogradely labeled cells in the thalamus (highlighted in gray) in case M3-FB-30/23a. Although the labeled cells are seen in every coronal section, their number differs significantly along the anterioposterior axis of the thalamus (see Fig. 5).

tex (mostly area 46 and, to lesser extent, with areas 9 and 9/46), the lateral parietal cortex (i.e., area PG), and the cortex buried in the superior temporal sulcus known as area TPO. The posterior cingulate areas are also highly interconnected with the parahippocampal formation. All these cortices have access to widespread cortical and subcortical networks (32), and it is, therefore, reasonable to assume that the PMC has the means to influence, and be influenced by, an extensive network of cortical structures involved in processing highly integrated and associative information. The extent of the PMC connectivity becomes even more widespread to involve other higher association cortical and subcortical networks when we take into account its connectivity with the thalamus, the claustrum, the caudate nucleus, and the cerebellum (via basis pontis).

Of special note is the pattern of PMC connectivity with the thalamus. Projections from areas 23a/b, 29/30, and 31, all of which are components of the posterior cingulate gyrus, target the associative nuclei in the dorsal thalamus in a continuous bar-like pattern. Each of these nuclei is in a cortico-thalamo-cortical loop with other higher association cortices. Thus, the PMC connections with these nuclei may provide a suitable anatomical means for this cortical region to partake in a more global information processing by orchestrating the activity of the loops operating through these nuclei. The finding of longitudinal labeling in the thalamus traversing its nuclear borders may perhaps indicate that there are functional building blocks within the thalamus extending across specific nuclear borders. It is important to note that the connectivity of the PMC with the thalamus is not reciprocal. There are thalamic areas that receive projections from the PMC without projecting back into it (Figs. 3–5). This nonreciprocal pattern may signify that there are thalamic nuclei that receive unidirectional information from the PMC to relay it further to other neural structures that PMC can or cannot reach directly, a hypothesis consonant with Sherman's view of the thalamic organization (33).

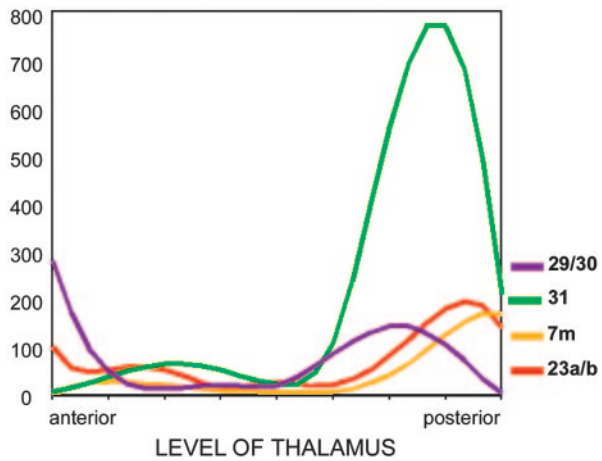

Fig. 5. Relative number of thalamic neurons projecting to different components of the PMC. The anterior-posterior gradient in thalamic projections is illustrated in different cytoarchitectonic areas of the PMC. For instance, when areas 29 and 30 were injected with a retrograde tracer, labeled thalamic neurons were predominantly found in the very anterior or posterior nuclei. By comparison, when area 31 was injected, only a few neurons were labeled in the anterior thalamic nuclei, but a much larger number of neurons were labeled in the pulvinar.

In 1977, Kievit and Kuypers (34) described a longitudinal band of retrogradely labeled thalamic neurons after multiple injections (as much as 15 μl) of horseradish peroxidase in the frontal cortex. In our study, the bar-like pattern was seen with the injection of as little as 0.5 μl of anterograde tracer in a single locus of the PMC. As noted in Figs. 4 and 5, the same longitudinal bar-like pattern was not seen after retrograde injections in the PMC. The density of retrogradely labeled neurons in the thalamus changes sharply across different nuclei. Furthermore, the location of the bar we have described for anterograde projections did not overlap with any of Kievit and Kuypers' bands in the thalamus.

PMC: Functional Unity and Diversity. Local interconnections among the components of the PMC and their connections with some of the same neural structures argue for a functional unity within the PMC. However, the fact that each of the areas within the PMC has its own particular set of connections with other neural structures suggests the presence of distinct functional modules operating within the PMC. For instance, the retrosplenial PMC (areas 29/30) distinguishes itself with its particular afferent inputs from the basolateral nucleus of amygdala and the orbitofrontal areas 11, 13, and 25 and efferent projections to the accumbens, the periaquaductal gray matter, and the reuniens, all of which are part of a network involved in emotional processing. It is therefore reasonable, as Maddock (10) has suggested, that one of the functions of the retrosplenial cortex is to partake in integrative emotional processing.

The connectivity pattern of areas 23a/b and 23c seems to be different. Based on previously obtained data by Morecraft and Van Hoesen (18), area 23c is connected with most of the cingulate gyrus, TPO, entorhinal cortex, dorsolateral prefrontal cortex, the prefrontal eye fields (area 8), and the opercular parietal area PO. However, it distinguishes itself from areas 23a and 23b on the basis of its connections with area 6, motor and sensory areas 3 and 4, and the secondary somatosensory cortex.

Similarly, area 7m distinguishes itself by its predilection for connections with frontal and cingulate structures involved in execution or planning of actions. It is also selectively connected with opercular and superior parietal lobules. Interestingly, we found that the connections of area 7m with area 6 involves the segment of this area that other functional studies have shown to be involved in the movements of the arm and hand i.e., the behavior of reaching or grasping objects. Moreover, area 7m distinguishes itself from the other PMC areas by the absence of its connections with ventromedial prefrontal/anterior cingulate areas 32, 24a, and 24b, and the periaquaductal gray matter. Unlike the posterior cingulate areas, the connections of area 7m with the hippocampal formation were sparse and targeted the presubicular area only.

Area 31 stands out as the only component of the PMC, which has efferent or afferent (or both) connections with all regions of the cingulate gyrus, superior and inferior parietal lobules, the frontal pole, entorhinal cortex, basal forebrain, basis pontis, and zona incerta. However, it should be noted that the widespread connections of Area 31 could be related to its location between areas 7m and 23.

Concluding Remarks. Based on our findings, although different components of the PMC have their own idiosyncratic connectivity pattern with other neural structures, strong interconnections among them and the shared connections of these components with some of the same brain areas support the hypothesis that they are functionally related to each other.

We believe that the functional role of the PMC relates to its afferent and efferent connections with the entire neural circuit to which it belongs. Our study provides a map of this circuit and, as such, it hopefully will serve as a useful tool for future studies aimed at uncovering the mechanisms by which the PMC operates within this neural circuit.

Materials and Methods

We injected tracers along the posterior medial surface of the brain in areas 23a and 23b, 29, 30, 31, and 7m (Fig. 1*f*). Area 23c was not included because data about its connections were available from previous research, including the ones originated from our own laboratory (18, 19). Eight young adult cynomolgus monkeys (*Macaca fascicularis*) were used in the study. Using sterile surgical procedures, we performed craniotomy on each animal and identified the injection target areas (Fig. 1) by relying on neuroanatomical landmarks. Anterograde tracers Biotinylated Dextran Amine (BDA) and Fluoro-Ruby (FR), and retrograde tracers Diamidino Yellow (DY) and Fast Blue (FB) were used (Table 1). After a 24- to 27-day period of survival, all monkeys were anesthetized with Nembutal and the brain was perfused transcardially with 0.9% saline followed by chilled 4% paraformaldehyde in 0.1 M phosphate buffer (PB) and flushed with 10% and then 30% sucrose in 0.1 M PB. The specimen were stored in 30% sucrose/0.1 M PB for 4 days at 4°C and sectioned coronally on a freezing microtome at a thickness of 50 μm. The brain sections were processed for the visualization of the tracers as described in *Methods* in *Supporting Text*.

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