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Thalamic and Cortical Afferents Differentiate Anterior from Posterior Cingulate Cortex in the Monkey

Abstract. *The anterior cingulate cortex receives thalamic afferents mainly from the midline and intralaminar nuclei rather than the anterior thalamic nuclei. In contrast, the posterior cingulate cortex receives afferents primarily from the anterior thalamic nuclei and from extensive cortical areas in the frontal, parietal, and temporal lobes. These contrasting afferents may provide a structural basis for pain-related functions of the anterior cingulate cortex.*

A wide range of clinical and experimental data indicate that anterior and posterior cingulate cortex are functionally distinct regions of the limbic system. These studies consistently demonstrate the involvement of the anterior cingulate cortex in many complex somatic and visceral motor functions as well as in responses to pain, whereas the posterior cingulate cortex has little to do with such functions. Thus, electrical stimulation of the anterior cingulate cortex (area 24) in the cat and the monkey produces cardiac slowing, piloerection, pupillary dilation, and changes in the rate of respiration and muscular tone (*1*). Stimulation of area 24 in humans also produces integrated motor responses (such as stretching and sucking) (*2*). Furthermore, stimulation of the anterior cingulate cortex in the cat inhibits attack behavior evoked by hypothalamic stimulation, whereas stimulation of the posterior cortex does not (*3*). In addition, ablation studies have shown that anterior cingulate lesions produce deficits in alternation learning, but posterior cingulate lesions do not (*4*). Of particular significance is that in humans neurosurgical procedures that interrupt axons coursing beneath the anterior cingulate gyrus alleviate the noxious effects of chronic pain although perception of pain per se is not abolished (*5*). This is interesting since the anterior cingulate gyrus has a much higher affinity for binding opiates than the posterior cingulate gyrus (*6*).

In light of these data, it is surprising that anatomical studies have not yet resolved the issue of precisely which thalamic or cortical areas send afferents to the cingulate gyrus. As a consequence, the available anatomical data do not provide a good structural basis for the extensive functional differences between the anterior and posterior areas of the cingulate cortex nor for the "pain-related" functions of the anterior cingulate gyrus. It has long been thought that the anterior, mediodorsal, and laterodorsal nuclei of the thalamus are the source of thalamic afferents to the cingulate gyrus, with separate divisions of the anterior thalamic nuclei sending afferents to both the anterior and posterior cingulate cortex, while the mediodorsal nucleus sends afferents to the anterior cingulate cortex and the laterodorsal nucleus to the posterior cingulate cortex (*7*). The ablation-degeneration techniques used in such studies are difficult to interpret, however, because the lesions usually damage adjacent fibers of passage (*8*).

Using anatomical techniques that avoid these problems, we have found that the anterior cingulate cortex receives afferents primarily from the midline and intralaminar nuclei rather than from the anterior thalamic nuclei. In contrast, the anterior and laterodorsal thalamic nuclei project to the posterior cingulate cortex. Furthermore, the anterior cingulate cortex receives few cortical afferents, while the posterior area receives extensive afferents from the frontal, parietal, and temporal lobes, maintaining the dichotomy of the thalamic afferents.

In eight rhesus monkeys (*Macaca mulatta*), a 20 percent solution of horseradish peroxidase (HRP) was injected into the cingulate gyrus. The results are based on four cases with injections of 0.14 μl each. These cases were processed according to the perfusion-fixation procedure described by Rosene and Mesulam (*9*) and were reacted with the tetramethyl benzidine reaction procedure of Mesulam (*10*). We tried to keep injections, postoperative survival time, and processing procedures identical to facilitate comparisons. Furthermore, none of the injections appeared to penetrate underlying white matter. Cytoarchitectural division of the cingulate gyrus into area 24 (anterior cingulate cortex) and areas 23 and 29 (posterior cingulate cortex) is based on Brodmann's cytoarchitectonic map (*11*) while parcellation of the thalamic nuclei is according to Olszewski (*12*).

After HRP was injected into the anterior cingulate gyrus (Fig. 1), only small numbers of HRP-labeled neurons were present in a few cortical areas, whereas posterior injections produced extensive labeling of neurons in a larger number of cortical regions. After injections into the anterior cingulate cortex, only a few labeled neurons were found in the dorsolateral prefrontal cortex, in the lateral orbitofrontal cortex, in the insular cortex, and in the caudal parahippocampal gyrus [areas TF and TH (*13*)] (Fig. 1). After posterior injections, however, large numbers of labeled neurons were found in the dorsolateral bank and depths of the principal sulcus, the medial orbitofrontal cortex, areas TF and TH of the parahippocampal gyrus, and in the posterior parietal cortex. The anterior cingulate cortex also contained labeled neurons, as did the posterior cingulate cortex after anterior injections, indicating a reciprocity of connections between the anterior and posterior cortices. For all these cortical areas, anterograde transport of ^{3}H-labeled amino acids confirms a projection to cingulate cortex areas 24, 23, or 29 distinct from adjacent frontal or parietal cortex into which HRP could spread. Afferents from both the amygdala and the hippocampus were also selective in their distribution to the anterior and posterior cingulate gyrus. Thus, the lateral basal nucleus of the amygdala sends afferents to area 24 anteriorly, while the subicular division of the hippocampus sends afferents to the posterior cingulate cortex (*14*).

Even more striking than the differences in cortical afferents to the anterior and posterior cingulate cortices is the contrast in thalamic afferents. Injections of HRP into the anterior cingulate cortex (Fig. 1) produced extensive labeling of neurons throughout the midline and intralaminar thalamic nuclei (Fig. 2, A to C). Surprisingly, these anterior injections failed to demonstrate HRP labeling of neurons in the anterior thalamic nuclei as expected. Instead, the most numerous and heavily labeled neurons were located in the midline and intralaminar nuclei including the paraven-

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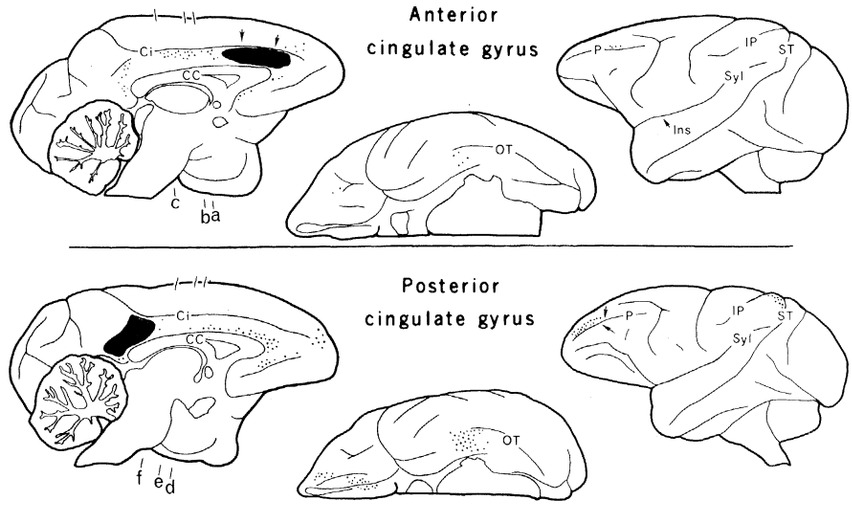

Fig. 1. Injections of HRP into the cingulate gyrus are indicated by the black shading on the medial surface view of the hemisphere. After both anterior and posterior injections were made, many HRP-labeled neurons were found throughout the remainder of the cingulate gyrus (labeled neurons in the depths of the sulci are indicated by arrows). After HRP injection into the anterior cingulate gyrus, only occasional labeling of cortical neurons was observed in the lateral orbitofrontal cortex, the parahippocampal gyrus [medial to the occipitotemporal sulcus (*OT*)], the dorsal bank of the principal sulcus (*P*), and in the insula (*Ins*) (arrow). After the posterior injection greater numbers of HRP-labeled neurons were found throughout wider regions of the cerebral cortex including the medial orbitofrontal cortex, the parahippocampal gyrus, the dorsal bank and depths of the principal sulcus, and posterior parietal cortex. Lowercase letters *a* through *f* indicate levels equivalent to (A) through (F) in Fig. 2. Abbreviations: *CC*, corpus callosum; (sulci) *Ci*, cingulate; *IP*, intraparietal; *ST*, superior temporal; and *Syl*, Sylvian.

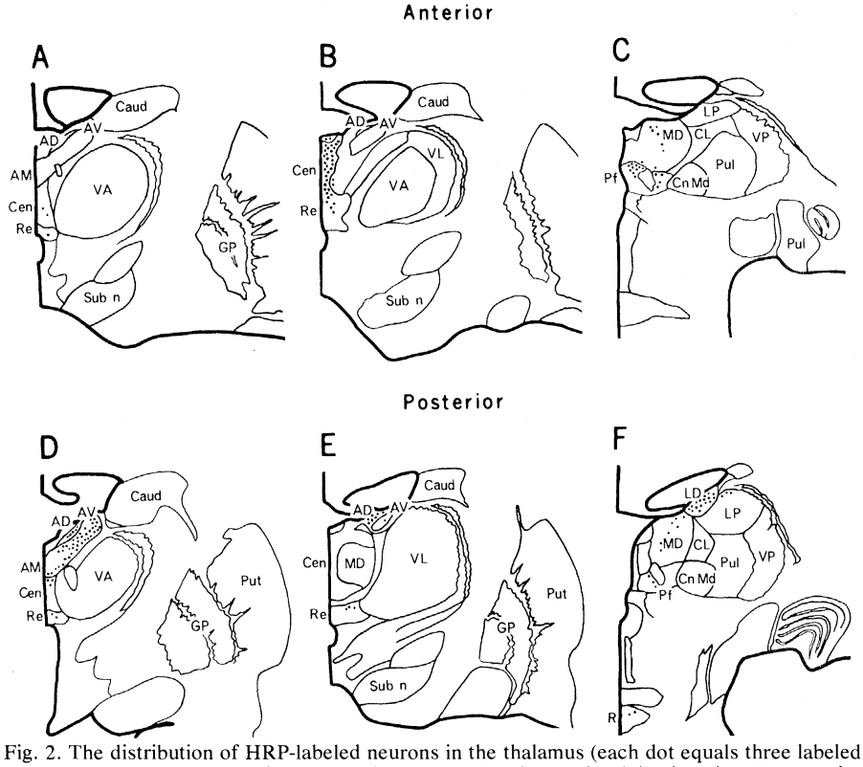

Fig. 2. The distribution of HRP-labeled neurons in the thalamus (each dot equals three labeled neurons) indicated at approximately equivalent levels (Fig. 1) after injections into the anterior and posterior cingulate gyrus. (A–C)The anterior injection produced extensive labeling of neurons in the central (*Cen*) and parafascicular (*Pf*) nuclei as well as in the reuniens (*Re*) and mediodorsal (*MD*) nuclei, but no labeling of neurons in the anterior nuclei. (D–F) The posterior injection produced extensive labeling of neurons in the anterior and laterodorsal (*LD*) nuclei; a few labeled neurons in the reuniens, parafascicular, and mediodorsal nuclei; and a few labeled neurons in the central nuclei. Abbreviations: *AD*, anterodorsal; *AM*, anteromedial; *AV*, anteroventral; *Caud*, caudate; *CL*, centrolateral; *Cn Md*, centrum medianum; *GP*, globus pallidus; *LP*, lateral posterior; *Pul*, pulvinar; *Put*, putamen; *R*, raphe; *Sub n*, substantia nigra; *VA*, ventral anterior; *VL*, ventral lateral; and *VP*, ventral posterior.

tricular, reuniens, parafascicular, central superior lateral, and central densocellular nuclei as well as the mediodorsal nucleus. In addition, many HRP-labeled neurons were found in nucleus limitans of the posterior thalamus, in the substantia innominata and claustrum of the forebrain as well as the dorsal and median raphe nuclei and the locus coeruleus in the brainstem. Injections of HRP into the posterior cingulate cortex (Fig. 1) produced a pattern of labeling that was strikingly different from that seen after the anterior HRP injections. Posterior injections resulted in extensive labeling in all the anterior thalamic nuclei (dorsal, ventral, and medial divisions) as well as the laterodorsal thalamic nucleus (Fig. 2, D–F), whereas only a few labeled neurons were found in the midline and intralaminar nuclei. Labeling in the posterior densocellular part of the mediodorsal thalamic nucleus as well as in the raphe nuclei and the locus coeruleus was similar to that observed after the anterior injections. Labeling in the rostral part of the mediodorsal thalamic nucleus and the substantia innominata of the forebrain was much less, while that in the claustrum was greater.

These results indicate that the cingulate gyrus can no longer be considered a homogeneous entity to which the various anterior thalamic nuclei project. Instead, the cytoarchitectonically distinct anterior and posterior cingulate cortices receive distinct sets of both thalamic and cortical afferents. The fact that the anterior cingulate cortex receives thalamic afferents from the midline and intralaminar nuclei while the more posterior cingulate cortex receives afferents from the anterior thalamic nuclei establishes an anatomical dichotomy between these regions of the limbic system. This dichotomy may provide a morphological substrate for some of the functional differences cited above.

Thus, several lines of evidence indicate that thalamic afferents to the anterior cingulate gyrus observed in this study may provide a direct route to the cortex for responses to pain. (i) A number of these nuclei including the mediodorsal and intralaminar nuclei receive afferents from the spinothalamic tract (*15*) which originates from cells that respond to peripheral pain stimuli. (ii) Many of the thalamic nuclei we have shown to project to the anterior cingulate gyrus have been demonstrated electrophysiologically to respond to painful stimuli [for example, parafascicular, mediodorsal, and limitans (*16*)]. Also, stimulation of the medial thalamus, including histologically verified placements in the

midline and parafascicular nuclei, produced analgesia and concomitant release of enkephalin-like substances in human patients (*17*). Third, pharmacological evidence indicates that both the medial thalamus and anterior cingulate gyrus have a high affinity for binding opiates (*6*, *18*) and that iontophoretic application of morphine to the medial thalamus as well as the parafascicular nucleus produces analgesia (*19*). Finally, although neurosurgical interruption of cingulate gyrus connections does not abolish the sensation of pain, it does eliminate its noxious aspects (*5*). Similarly, lesions in the medial thalamus and intralaminar nuclei also relieve the affective response to pain (*20*). Furthermore, other afferents to the anterior cingulate gyrus may also be involved in pain-related activity, for example, the amygdala and insula have a high affinity for binding opiates (*18*). Besides this direct evidence implicating the anterior cingulate gyrus and its thalamic and cortical afferents in pain-related activity, the anterior cortex may also be involved in reflex responses to painful stimuli. Thus, pupillary dilation, piloerection, and some forms of shrill vocalization can be produced by stimulating the anterior but not the posterior cingulate gyrus (*1*).

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Honey Caches Help Female Paper Wasps (*Polistes annularis*) Survive Texas Winters

Abstract. Polistes annularis *females store honey in their nests in autumn. They return to their nests on warm winter days, eat honey, and defend it from non-sisters. Honey deprivation decreases numbers surviving the winter; females that do survive without honey build smaller spring nests.*

Polistes annularis exhibits a newly discovered behavior, winter honey caching. Previously, only large perennial colonies of social insects have been reported to make and store honey for use as food during periods of drought or cold weather (*1*, *2*). Females of *P. annularis* abandon their nests after caching winter stores of honey and retreat to hibernate in more protected places. On warm winter days females leave hibernacula, return to natal nests, and feed on their honey. At this time they will defend it against non-sisters. Dependence on honey stored overwinter has a decisive impact on the social biology of *P. annularis*, for it necessitates proximity of hibernacula to nests and continued contact and cooperation between sisters. This facilitates springtime recognition of sisters who cooperate in building new nests near the natal nest.

Although winter honey caching is previously unreported in polistine wasps, honey manufacture and storage of small droplets in the nest in cells occupied by eggs or small larvae is common (*2*–*5*). Honey droplets have been seen in nests at all seasons, as long as the wasps are on the nests.

Winter honey caching was observed in a population of *P. annularis* along a 15-m high limestone cliff overlooking a reservoir, Lake Travis, 26 miles west of Austin, Texas. Nests were extraordinarily common along this particular west-facing cliff; more than 1000 nests were found along a 200-m section. In 1976, 40 nests were observed, and all autumn reproductive males and females were marked with enamel (*6*). Reproductive females were distinguished from workers by their lack of wing wear (*7*). Honey first began to appear in quantity in empty cells in September. By November, all nests still occupied had some honey, and most had all cell walls coated with a thick layer of honey similar in taste to that of honeybees, but much more viscous. In November, females began entering a crack in the cliff and abandoned mud cliff swallow nests, searching for places to hibernate. When nights were cooler than 5°C, wasps spent them in hibernacula, returning to their nests on sunny warm days. On the nest they fed on honey and repelled all intruders not marked as sisters. Commonest among intruders were other wasps from the same population, often bearing marks indicating that they were born on other nests. These were fought off vigorously and chased (*8*). In addition, other insects tried to steal honey. Several *Vespula* sp. were successful, although they were chased off immediately when discovered. Three low nests were knocked down by a raccoon that shredded them in the process of consuming honey.

Only a small amount of honey loss was endured by *P. annularis* and several factors appeared to be contributory. Most of the nests are inaccessible to mammals in that they cannot walk up overhanging rock faces. Wasps defend the nests on warm days so that other insects have little chance of stealing successfully. Nest predation by birds for honey does not occur (*9*).

Winter visits to the study site revealed conditions necessary for females to leave their hibernacula. Females returned to their nests on days that reached at least 21°C with at least 110 minutes of sun, and on overcast days when the temperature was at least 26°C. Warm days as defined above were counted for every 15-day period in November through February for the past 13 years (*10*). Each of the 15-day periods examined had a mean

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