THE CINGULATE GYRUS:
ADDITIONAL MOTOR AREA AND CORTICAL AUTONOMIC REGULATOR

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TEN FIGURES

This study was made to explore a cortical region that developed to a high degree in animals which are dependent upon large olfactory connections. The cingulate gyrus has remained a sizeable cortical convolution in primates and a few other mammals in which the olfactory pathways are small or vestigial. This gyrus (fig. 1, A) encircles the subdivisions of the corpus callosum, extending from the sulcus of the corpus callosum to the sulcus cinguli. The anterior portion of the gyrus (Walker-Brodmann areas 24, 25; Walker, '40) contains agranular cortex (Rose and Woolsey, '48) similar to the motor area of the precentral gyrus. The authors just quoted described the posterior portion of the gyrus (areas 23, 29 and isthmus) as possessing granular cortex similar to the sensory area of the postcentral gyrus.

METHODS AND MATERIALS

The observations and testing of 16 *Macaca mulatta* monkeys included an evaluation of the certain items preoperatively and postoperatively. These items were temperature, pulse and respirations, conscious level, sensory modalities, motor and secretory activity and emotional behavior.

Ether anesthesia was employed for the operative procedure. After loss of consciousness, the head of the animal was prepared by shaving and cleansing with detergent, water, 70% alcohol and zephiran solution. Skull openings were made by dental drill points and rongeurs. No repair was made of the bone defect. Hemostasis was accomplished by ligature, electrocoagulation and application of gelfoam. The approach to the
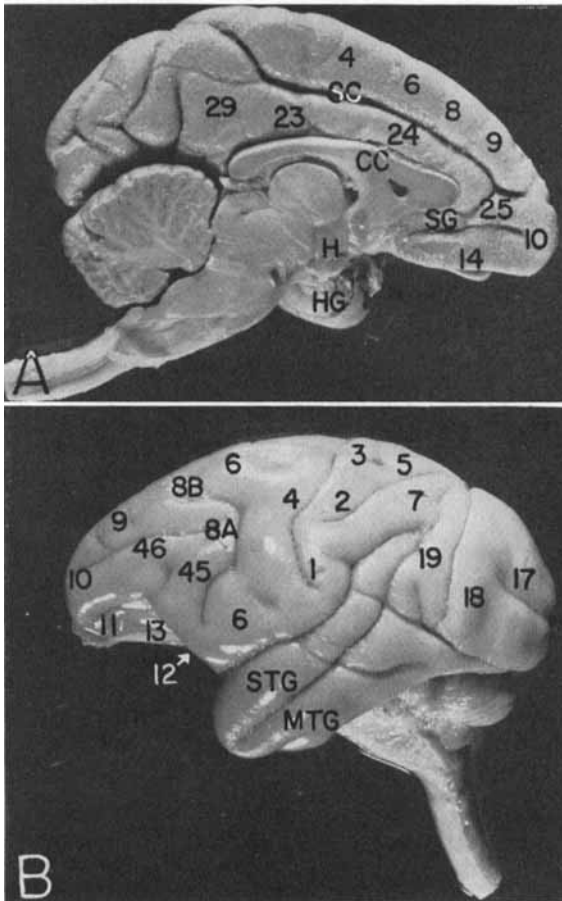

Fig. 1 A, Photograph of the medial surface of a macaque brain with Walker-Brodmann areas indicated. × 0.6. B, Photograph of the lateral surface of a macaque brain with Walker-Brodmann areas indicated. × 0.6.

cingulate gyrus was complicated by thrombosis of the single anterior cerebral artery with subsequent death of tissue. It was difficult to expose the cingulate gyrus for stimulation without unintentional trauma to the cortical regions forming the superior part of the horizontal fissure. In most of the animals, the superior cortical convolution was ablated in order to section the falx cerebri and obtain visualization of an intact cingulate gyrus. Repairs of dura, subcutaneous tissue and skin were made by nylon thread. A small cotton sponge was sutured to the skin and sealed by collodion to protect the incision. Surgical aseptic technique was utilized throughout.

Cortical areas were stimulated by monopolar electrodes of silver wire 15 mm long and 0.75 mm wide, insulated by polyethylene tubing. A metal rectal plug constituted the indifferent electrode. A Grass stimulator (model S4B), adjusted to deliver a square wave with a frequency of 40 per second duration of one millisecond, intensity of one to 14 volts, constituted the stimulus. Minimal and maximal strengths of current required to produce a particular motor activity were ascertained. These varied somewhat for the different animals used.

The microscopic slides resulting from the experimental work were prepared by the Swank-Davenport ('35) modification of the Marchi method. The animals were sacrificed at the end of a two to 4-week period dating from the completion of the experimentation. Under sodium pentobarbital anesthesia the thorax was opened and the aorta cannulated by way of the left ventricle. Perfusion of the arterial system with approximately 500 cm^3 of 10% formalin was carried out. The brain was removed and placed in 10% formalin to complete its fixation. Examination of the resulting slides revealed degenerated myelinated fibers with the artefacts such as described by Smith ('56). It was common to note such artefact in any of the cranial nerve roots, anterior olfactory nucleus, optic chiasma, lateral geniculate nucleus and the posterior commissure. Occasionally, artefact was found in the septohippocampal nucleus, precommissural fornix and preoptic area.

PROTOCOLS

Animal C-S-6, a small female macaque weighing about 2.2 kg, was operated upon on September 27, 1957. Stimulation of the left posterior cingulate areas was done in a caudorostral direction. At the first point stimulated, the pupils of the eyes were dilated, with the greatest dilatation present in the right eye (fig. 4, D). A vertical nystagmus occurred in which the quick component was upward, the eyelids were opened and the eyes were directed upward. The upper lip was retracted and the jaw had opened. From the area next stimulated, there resulted bilateral movements of the upper extremity, dominantly contralateral, clonic flexion and extension at the shoulder, the elbow, the wrist, and the metacarpophalangeal articulations (fig. 4, B, C). The muscles of the chest and abdomen were alternately contracted and relaxed. From the last area stimulated on the cingulate gyrus, the lower extremities followed the same pattern of movement as the upper extremities and these movements were also dominantly contralateral. As the strength of the stimulation was taken to 7 volts, a generalized convulsive seizure resulted. A small lesion was placed in the region where the stimulation had given rise to movements of the eyes.

At the completion of the surgical procedure, the animal's body felt cold to touch and the rectal body temperature was 30.9°C. There was intense shivering for 30 minutes while the body heat was slowly regained. The left palpebral fissure was narrow and the left side of the mouth retracted in contrast to the right side of the face. This right facial weakness persisted for two days. C-S-6 had conspicuous difficulty in sustaining upright posture without looking at her hands and her feet, and frequently re-establishing the grip of both her hands and her feet. She was hyperkinetic to the date of sacrifice in terms of numerous attacking, pacing, and climbing movements. She would pull at her bandage and rub her face frequently. There was almost constant vocalization with sounds which have characterized scolding and disagreeable dispositions in other monkeys.

When the brain was examined at necropsy the right superior frontoparietal convolution (fig. 1, B) of areas 4, 3 and 2 had been ablated. Some evidence of trauma was present at the 23–24 transition on the right, and a small lesion was present in the left areas 23 and 29 (fig. 1, A). Most of the destruction was in the right and the left superior frontoparietal convolutions, and minimal destruction was evident in right and left posterior cingulate areas.

The Marchi preparation appeared to be good except in corona radiata and the dorsal one-third of the posterior limb of the internal capsule in some blocks of tissue. There were no regions of the cortical laminae into which appreciable terminal degeneration could be followed. The

larger more heavily myelinated fiber paths of the frontoparietal con-
volution are more conspicuous than the small, lightly medullated fibers
of the cingulate gyrus.

Fiber paths can be followed from the superior frontoparietal con-
volution into the middle frontal (areas 8, 45, 46) and inferior parietal
(area 5) convolutions as the adjacent gyri (fig. 1). These fibers have
passed through the corona radiata of the same and opposite sides and
crossed though the body, the rostrum and the genu of the corpus cal-
losum. Some of the fibers in the corona radiata enter the superior
longitudinal fasciculus on the right and left to travel a considerable
distance. From the superior longitudinal fasciculus, a portion of these
degenerating fibers enter the pathways of the opercular region (areas
4, 6, 1) of the frontal and parietal lobes. Another portion descends
in the external capsule to the orbital region (areas 12, 13) of the
frontal lobe. Some crossed and uncrossed fibers from the lesion pass
through the rostrum of the corpus callosum toward the gyrus rectus
(area 14).

There are connections from the superior frontoparietal gyri to the
superior, the middle, the inferior temporal gyri and the hippocampal
gyrus. From the lesion, fibers can be followed through the corona
radiata to the superior longitudinal fasciculus and into the complex
that eventually separates into internal, external and extreme capsules.
The degenerating fibers that enter the external capsule are directed
into the inferior longitudinal fasciculus and toward the inferior temp-
oral and hippocampal gyri. Some of these cross to the other hemisphere
in the anterior commissure. An equally large portion of the fibers tra-
verse the extreme capsule to the superior and the middle temporal
gyri. There appear to be fibers decussating in the body of the corpus
callosum that enter the superior longitudinal fasciculus for this de-
scending course.

The superior frontoparietal convolutions connect with the cingulate
gyrus.

The connecting fibers travel medially from the frontoparietal con-
volution to a lateral position in the cingulum (fig. 5, A). There is some
suggestion of fibers following this same pathway from the cingulate
gyrus to the superior frontoparietal convolution (fig. 5, B). A few
degenerating fibers, that may be from the cingulate gyrus, are present
in the cingulum as it passes over the genu of the corpus callosum and
is directed toward the region of the subcallosal gyrus. There are some
very small calibre fibers which travel the posterior limb of the internal
capsule through the comb bundle into the pars reticulata of the sub-
stantia nigra on both sides (fig. 6, B). The small size of the fiber tends
to relate it to the cingulate.

Very few, fine, small degenerating fibers from superior frontopari-
etal gyrus appear to terminate in the caudate gyrus nucleus and the
putamen. A small number of degenerated fascicles that have passed
through the anterior and posterior limbs of the internal capsule and
the external capsule end in the globus pallidus.

Relative to the dorsal thalamus, a few degenerating fibers can be
observed passing from the cingulate lesions through the cingulum into
the corona radiata and thence to the anterior thalamic radiations.
Then, as the posterior limb of the internal capsule appears, these swing
dorsal to the capsule, ventral to the caudate nucleus, and through the
stratum zonale into the capsule of the anterior nuclear group (fig. 7).
They are most apparent in the nucleus anteroventralis. A few of
these fibers appear to enter the diencephalic periventricular system.
Numerous fibers of heavier calibre stream through the posterior limb
of the internal capsule, through the nucleus reticularis, the eternal
medullary lamina of the dorsal thalamus and into the field of the
ventral nuclear group. These can be followed caudally into the right
and the left red nuclei of the midbrain.

There are some fine, small degenerated fibers in the lateral and the
posterior hypothalamic areas. The direction of fibers suggests that
some have arrived by way of the diencephalic periventricular system
(fig. 7). More appear to turn ventromedially into the hypothalamus
from the cortical components in the position of the ansa and fasciculus
lenticularis as they collect in the field of Forel (figs. 8, C; 9, C, D;
10, A, B).

Degenerated cortical fibers from the superior frontoparietal con-
volution, and possibly from the cingulate gyrus, have passed into the
corona radiata to the posterior limb of the internal capsule across the
dorsal surface of globus pallidus in the position of the lenticular fas-
ciculus into the field of Forel. Another group of degenerated cortical
fibers which have entered the external capsule from the corona radiata
accompany the course of the ansa lenticularis. These swing dorsally
through the globus pallidus to join those in fasciculus lenticularis
at the tip of the medial segment of globus pallidus (fig. 9, A, B).
After what appears to be multiple synapses in the field of Forel (fig.
9, C, D), a group of degenerated fibers can be traced into the ventral
and the lateral tegmental areas of the midbrain (figs. 9, E, F;
10, C, D), the interstitial nucleus of the medial longitudinal fasciculus
and the nucleus of the oculomotor nerve.

Animal C-8-7, a male macaque weighing about 1.3 kg, was operated
upon on October 1, 1957. Stimulation of areas 23, 29 and the isthmus
proceeded in a rostrocaudal direction. From the first region of stimu-
lation there resulted bilateral movements of the facial musculature

which caused the eyes to close and the jaws to open. The head was thrust forward. Both upper extremities alternately flexed and extended at the shoulder, elbow, wrist and metacarpophalangeal joints. When the next area was stimulated, it was possible to observe a turning of the head toward the contralateral side (fig. 4, D). Although both of the eyes were closed, the movements of the facial musculature tended to be homolateral (fig. 4, B, C). Following stimulation of the third region, the head nodded upward and downward, the eyes were closed and there was a slight deviation of the head and neck toward the contralateral side.

Temperature measurement at the completion of the procedure indicated a drop of 3.7°C. Intense shivering lasted 40 minutes while the body heat slowly returned. The pupils of the eyes were widely dilated and the dilatation was greater in the pupil of the contralateral eye (fig. 4, D). A noticeable, generalized piloerection (fig. 4, E) had occurred. The head, neck, and eyes were deviated forcibly toward the homolateral side. This animal had a tendency to be sleepy for about three days. Alternating with the drowsiness was a marked hyperactivity during which he would frequently turn the head upon the neck. This monkey vocalized along with general body movements.

Examination of the brain at necropsy confirmed the operative procedure in which lesions had been placed in the first and third areas stimulated on the right cingulate gyrus. The rostral lesion lay in area 23 under the postcentral gyrus and the caudal lesion was at the isthmus. There was an extension from this latter lesion into the body and the splenium of the corpus callosum, the right fornix, and the nucleus medialis, the nucleus lateralis dorsalis and the nucleus ventralis lateralis of the dorsal thalamus. Below the nucleus ventralis lateralis a band of the lesion crossed the posterior limb of the internal capsule, cutting into the medial segment of the globus pallidus (fig. 8, A). Areas 3, 2 and 5 had been ablated in the left superior parietal convolution (fig. 1, B). Packing for hemostasis on the left side had caused some compression damage of the left posterior cingulate area in the region of the isthmus (fig. 1, A).

The Marchi preparation appeared to be adequate throughout most of the blocks of tissue. Some of the slides lacked complete penetration of the right and the left limbs of the posterior portion of the internal capsule which extended upward across the corona radiata into a part of the superior frontal radiation. The last block of tissue possessed a large proportion of artefact. These factors were taken into account in evaluation of the results of the microscopic study. At no point is it possible to trace fibers unequivocally into the cortical laminae. The

degenerating fibers from the parietal convolution appear to be larger and better medullated fibers than those from the cingulate gyrus.

Fiber paths from the one cingulate gyrus connect to the side opposite by way of the cingulum and the body of the corpus callosum (fig. 5, B). This intercingulate path is greatest at the level of the lesion. There is the suggestion that a very few fibers from the posterior cingulate region travel rostrally in the cingulum, cross in part through the corpus callosum and then curve bilaterally over the genu of the corpus callosum toward the subcallosal gyrus. The cingulum on the right appears to have greater quantitative degeneration and larger fibers than that on the left. This gives some foundation for postulating connections from the superior parietal convolution (areas 3, 2, and 5) toward the posterior cingulate gyrus similar to the connection illustrated in figure 5, A.

A large mass of fibers emerge from the anterior limb of the internal capsule on the right, pass toward the superior frontal convolution (areas 4, 6, 8) and toward the middle and inferior frontal convolutions at the level of the superior and inferior rami of the arcuate fissure into areas 8, 45, 46 (fig. 1, B). There is some distribution of these fascicles through external and extreme capsules, and subsequently toward the orbital surface of the frontal lobe into areas 12 and 13. It is possible to trace this group of fibers, which are not present in the left hemisphere, caudalward into the anterior thalamic radiations. From their source in the dorsal thalamic lesions numerous fibers extend diffusely through the lateral and ventral thalamic nuclear fields. These accompany fibers which are passing over the stratum zonale ventral to the caudate nucleus and which enter the anterior thalamic radiations (fig. 7) to project to the hemisphere.

There are degenerating fibers from the lesions into the superior, the middle, the inferior temporal gyri, the hippocampal gyrus, the basolateral amygdaloid nucleus, and the hippocampus of both sides. Most of the degeneration in the temporal lobes is in a vertical axis with the lesions. Since it is more conspicuous on the left, it suggests that the cingulate lesions and the left parietal lesion are contributing to these fibers paths. Degeneration leading into the amygdaloid nucleus and the hippocampus, however, is somewhat greater on the right side. It should not be overlooked that some of the degeneration in the rostral portion of the temporal lobe and the amygdala may have reached the external and extreme capsules from the anterior thalamic radiations. This involves the superior temporal gyrus and the basolateral portion of the amygdala, primarily. Degenerating fibers from the external capsule enter the anterior commissure in the region of the amygdaloid nuclei. As the hippocampus appears, there are fibers present in the

alveus on both sides and in the fornix on the right. In both hippo-
campi terminal degeneration can be found around the pyramidal cells.

In the septal region there are degenerated fascicles in the precommis-
sural fornix. They could be followed from there principally to the
lateral septal nucleus on the right. Some fibers do extend downward
into medial septal nucleus and the islands of Calleja. A few fibers per-
forate the body of the corpus callosum to reach the right induseum
griseum. Some degenerated fibers are present in the left lateral septal
nucleus.

Both caudate nuclei receive a few degenerating fibers from the sub-
callosal bundles. There is some evidence that a few fibers travel from
the lesion in the dorsal thalamus over the stratum zonale to enter the
caudate nucleus along the medial surface after perforating the stria
terminalis, or ventrally as the anterior thalamic radiations are form-
ing. Globus pallidus of both sides presents a large amount of degenera-
tion as the genu becomes the posterior limb of the internal capsule. It
seems likely that some of the fibers which have reached the globus
pallidus have come from the cortical lesion by way of the posterior
limb of the internal capsule. The dorsal portion of the left claustrum
appears to receive degenerating fibers through the external and the
extreme capsules. Comparison with the fibers on the right suggests
that the source of the fibers entering the claustrum is from the area
involved in the lesion in the superior parietal convolution.

In the dorsal thalamus the anterior nuclear group receives degener-
ating fascicles that appear to turn out of the cingulate gyrus into the
cingulum, then pass to the corona radiata and into the anterior thala-
mic radiations. As the posterior limb of the internal capsule appears
(fig. 7), these radiations travel dorsal to it and ventral to the caudate
nucleus, through the stratum zonale to the capsule of the anterior nu-
clei. The termination of the fibers is apparent in the nucleus antero-
ventralis and the nucleus anterodorsalis on the right side. A very few
fibers follow the same route and terminate contralaterally. The de-
generating fibers which have entered the anterior thalamic radiations
have been described (p. 236). From the medial nucleus there are some
very small, lightly medullated fibers which turn medially to become
components of the diencephalic periventricular system ending in the
hypothalamus around the anterior hypothalamic area and the peri-
ventricular nucleus. More heavily medullated fibers from the medial
nucleus collect in the internal medullary lamina. A proportion of these
reach the intralaminar nuclei. Some fibers, however, appear in pars
medialis and pars lateralis of the nucleus ventralis posterior. Other
fibers extend rostrally into the nucleus ventralis lateralis. In the ex-
amination of the microscopic slides there is evidence of a little com-

pression damage in the dorsomedial tip of the right pulvinar. From this site a group of fibers collects lateral to the internal medullary lamina and turns downward into the pretectal region of the midbrain. A small lateral corner of the right stria medullaris thalami was amputated in the course of the lesion. Some degenerated fibers are traced from this point into the habenular nuclei.

In addition to the termination of the degenerated fibers of the diencephalic periventricular system, there is degeneration of the right mammillary body from the ending of the pathways of the severed fornix. The pallidohypothalamic tract on the right can be seen coursing toward the ventromedial hypothalamic nucleus.

There are fibers in the postion of the lenticular fasciculus and ansa lenticularis on both sides. Those from the left are very fine, small, lightly medullated fibers. These may be from the cortical lesion. Those on the right are large, coarse, and well medullated (fig. 8, A). These latter fibers can be followed from the lesion in the medial segment of the globus pallidus as they form both the ansa and the fasciculus lenticularis. The two paths converge into a common bundle. On each side there seems to be synapse in the nucleus of the field of Forel (fig. 8, A, C). And, on both sides, some fibers can be followed to the tegmentum of the midbrain (fig. 9, E, F), the medial longitudinal fasciculus and the nucleus of the oculomotor nerve. There is heavy bilateral degeneration in the substantia nigra, pars reticulata and pars compacta. The fine nigral fibers interdigitate with fascicles of the comb bundle and appear to have come from the posterior limb of the internal capsule (fig. 6, B). It is probable that they are from the cortical lesions. As the most caudal portion of the cortical lesion appears, some degenerating fibers enter the retrolenticular limb of the capsule, passing diffusely over the pulvinar, end in the tegmentum and red nuclei of the midbrain.

Animal C-S-8, a 1.3 kg female *Macaca mulatta,* was operated upon on October 4, 1957. In the stimulation which was oriented from a rostral to a caudal position on the middle part of the cingulate gyrus (fig. 1, A), three general regions were explored with the electrode. As the first position was stimulated there appeared bilateral contraction of the musculature of the face, and alternating tonic flexion and extension of the contralateral lower extremity. When stimulation was applied directly below this point, the facial movements were more dominantly homolateral and some of the musculature of the shoulders was activated. Following stimulation of the second position, there were bilateral facial and left lower extremity movements again. After stimulating the third position, both lower extremities and the tail were set in motion. Facial movements tended to be homolateral as the electrode

was moved directly below the third position. A lesion was placed in the whole area explored by stimulation.

There was a 3.9°C drop in the animal's temperature, and marked shivering was evident at the end of the surgery. The tendency of the animal to be sleepy alternated with activity. Her hands were held in an athetoid position. The head and the neck deviated homolaterally and the pupil of the left eye was comparatively larger than that of the right eye. A right hemiparesis involving the face, the arm, and the leg persisted approximately two weeks. Although the sleepiness diminished progressively, this animal would yawn and become drowsy for 13 days postoperatively. Immediately after the surgical procedure there was an increase in the vocalization of C-S-8 which persisted to the date of sacrifice. There were frequent attacking movements accompanied invariably by angry cries (fig. 4, E) characterizing this monkey's behavioral pattern.

Post mortem examination of the brain showed a lesion which had been enlarged by hemorrhage in the right cingulate gyrus (fig. 1, A). It extended from the level of area 6 to the isthmus region. This included areas 23 and 24. There was minimal cortical damage on the medial surface of the brain in areas 6 and 4. On the left side, the cortex had been ablated over areas 4, 6, 8 (fig. 1, B). The left cingulate gyrus had been injured by compression of edema, fluid and blood. The Marchi series was good throughout. Fine, small, degenerating fibers extend rostrally from the lesion into the cortical radiations, but not visibly into the laminae.

Degenerating fibers in the cingulum on both sides turn around the edge of the genu of the corpus callosum and travel ventralward in a position medial to the rostrum of the corpus callosum. These fibers are going to the subcallosal gyrus bilaterally. There appear to be short connections (fig. 5) from the superior frontal convolutions (areas 4, 6, 8) in the cingulum, and from the cingulate gyrus to the superior frontal (areas 6, 8) and parietal (areas 3, 2) convolutions. Intercingulate connections extend from the cingulate gyrus of one side into the cingulum, then to the body of the corpus callosum and then to the cingulum and the cingulate gyrus of the contralateral side.

Fascicles that are degenerating can be observed in the corona radiata. These distribute into the frontal pole, (areas 9 and 10) the superior frontal convolution, (areas 6, 8, 4) middle frontal convolution (areas 46, 8) and particularly to the frontal operculum (areas 45, 4) and orbital gyri (areas 12 and 13). These fibers traverse the external and the extreme capsules when they are in the field. In a comparable manner, there are connections to the superior (areas 3 and 2) and inferior parietal (areas 1 and 2) convolutions as they

appear. It is probable that most of this pattern consists of the distri-
bution of fibers from the lesion in the superior frontal convolution to
the gyri of the same and the opposite hemispheres. The microscopic
evidence does not preclude the possibility of some source of the pattern
from the cingulate gyrus too.

There are fascicles from the lesions in the superior, the middle and
the inferior temporal gyri, the hippocampal gyrus and the hippocam-
pus. These connections can be traced from the lesions through the
corona radiata to the complex that separates into the internal, the
external and the extreme capsules. The degenerating fibers that enter
the external capsule are directed into the inferior longitudinal fas-
ciculus and toward the inferior temporal and the hippocampal gyri.
Some fibers cross from the external capsule to the opposite side by way
of the anterior commissure. Those fascicles which enter the extreme
capsule are directed essentially into the superior and the middle tem-
poral gyri. Some of the fibers which have entered the hippocampal
gyrus can be traced into the alveus toward the hippocampus. As the
cingulum turns ventralward, medial to tapetum (figs. 8, B) to enter
the temporal lobe an appreciable quantity of degeneration follows this
route into the alveus. Another portion of the fibers in the cingulum
have interdigitated with those of the splenium of the corpus callosum
and entered the fornix. A number of these will be found decussating
in the posterior hippocampal commissure to reach the contralateral
fornix. In both fornices the degenerated fascicles pass ventralward
toward the hippocampus.

In the septal region it is possible to observe slight degeneration in
the precommissural fornix. This degeneration extends into the septo-
hippocompal nucleus, the medial septal area, and the islands of Calleja.
It appears to be related to intrusion of the lesion into the induseum
griseum and the corpus callosum where perforating fornix fibers are
found.

There is degeneration present in the caudate nuclei. It is greater on
the left than on the right side. Some of the degenerated fascicles have
reached the caudate nucleus by the subcallosal bundle, but more fas-
cicles have come by way of anterior and posterior limbs of the internal
capsule. In all instances there appears to be a loss of myelination of
the fiber shortly after entry into the caudate nucleus. The nucleus
accumbens has a very small amount of degeneration that traverses the
external capsule. The putamen on the left side receives degenerated
fascicles from the external capsule and the anterior limb of the internal
capsule. It is possible to find degenerating fibers entering the globus
pallidus of the right and left sides by the same routes as those to the
putamen, and also through the posterior limb of the internal capsule.

From the cingulate gyri, degenerating fibers pass bilaterally into the cingulum, thence to the corona radiata and through the anterior thalamic radiations, over the anterior limb of the internal capsule, to turn ventral to the caudate nucleus (fig. 7). They then pass over the stratum zonale to enter the anterior nuclear groups of the dorsal thalamus. The greater portion of the degeneration is in the anteroventral and anterodorsal nuclei. Some of the fibers in the capsule of the anterior nuclear group bypass the group to enter the stria medullares of the thalamus. These can be followed into the habenular nuclei of both sides. A few of these same fibers continue on through the stria medullaris into the diencephalic periventricular system. In the caudal portion of the dorsal thalamus degenerating fascicles that have come through the anterior thalamic radiations enter the medial nucleus (particularly the left one), nucleus lateralis dorsalis (particularly the right one), and the dorsolateral portion of the right pulvinar bilaterally. Numerous degenerated fibers enter the lateral and ventral nuclear groups by way of posterior limb of each internal capsule, through the reticular nuclei and across the external medullary laminae. Many of these appear to be fibers of passage, but some also terminate in the respective nuclei. This is noticeably evident in the nucleus ventralis lateralis on the left side.

Anterior hypothalamic areas on the right and left sides receive some degenerating cortical fibers that have traveled ventromedially with the ansa lenticularis. Lateral and posterior hypothalamic areas and the ventromedial hypothalamic nuclei receive some comparable fascicles from the position of the lenticular fasciculi (figs. 8, C; 9, C, D; 10 A, B). Throughout the hypothalamus a very few of the finely medullated fibers in the diencephalic periventricular systems can be seen traveling ventralward toward the nuclear groups close to the ventricle.

Along the course of each ansa and fasciculus lenticularis there are an appreciable number of degenerated fibers which are of cortical origin (fig. 9). On each side, these fibers can be followed through the formation of the ansa and fasciculus lenticularis into their convergence in the field of Forel. A few fibers can be traced into ventral (fig. 10, C, D) and lateral tegmental areas of the midbrain, the interstitial nucleus of the medial longitudinal fasciculus and the nucleus of the oculomotor nerve. Another large group of fibers reaching the midbrain are those already mentioned in the ventral and lateral nuclear groups of the dorsal thalamus. These pass ventralward and into the red nucleus. As the pulvinar comes into the thalamic field a different course can be observed in these degenerating fibers that have cortical origin and have entered the thalamus from the posterior limb of the

internal capsule. They travel with the internal corticotectal paths and diverge sharply into inverted y branches in the pretectal region of the midbrain. The inferior branch of the y passes directly medial to the medial geniculate nucleus mingling with the fibers of the medial lemniscus and thence to ventral and lateral tegmental portions of the midbrain (fig. 9, E, F). The superior branch of the y enters the posterior commissure and ends contralaterally in the red nucleus, the medial longitudinal fasciculus and the oculomotor nucleus. This group of fibers in the position of the internal corticotectal path is more prominent on the right side where the lesion in the cingulate gyrus is also larger. A portion of the degeneration in the posterior limb of the internal capsule interdigitates with the fibers of the comb bundle and terminates in the pars reticulata and the pars compacta of the substantia nigra bilaterally (fig. 6, B). The larger calibre fibers in the posterior limb of the internal capsule have entered the cerebral peduncle and basis pons bilaterally in the positions of corticospinal and frontocorticopontine tracts.

Animal C-S-9, a small male macaque, about 1.4 kg in weight, was operated upon on October 7, 1957. Stimulation of the left subcallosal gyrus, area 25, and rostral area 24 was carried out in a caudorostral direction (fig. 1, A). Movements of the upper extremity and face resulted from the first cortical stimulation. At the dorsal portion of the gyrus upper extremity movements tended to be bilateral and at the ventral depth of the gyrus, contralateral. Facial musculature changes were essentially bilateral. As the stimulus was applied more rostrally, bilateral upper extremity movements and bilateral facial muscular contraction were still evoked. The former activity was diminishing in magnitude, although still apparent in the shoulder musculature. In the third region stimulated, near the genu of the corpus callosum, facial muscle contracted on both sides, head and eyes were directed upward and backward. Proceeding even more rostralward with stimulation, the head and the eyes were directed downward and forward. Although the eyes were closed, their direction and alternating pupillary dilatation could be noted when the lids were forcibly held open. As the stimulation contacted the subcallosal gyrus, sialorrhea occurred. Respiratory irregularity was marked from the stimulation in this region. Noisy respiration with forced expiration progressed into vocalization and then into apnea.

There was a profound drop (4.0°C) in rectal body temperature from 38.4°C to 34.4°C at the end of the surgery. Shivering was present and continued about 30 minutes. This animal was extremely vocal with angry overtones in the sounds produced. The vocalization was present as soon as the animal reacted from the anesthesia and

thereafter until sacrifice. Piloerection was marked, and also sustained during the period of observation. A fine tremor of the head and the neck and apraxia of the left upper extremity subsided in two days. Dysmetria of the face because of a left facial weakness was apparent in the two and one-half weeks of observation. Transient sleepiness occurred for three days. Alternating with the sleep were numerous noisy motor activities. This monkey pulled at his bandage, rubbed his face, and paced his cage more than other operated animals.

At necropsy it was found that the cortex of areas 10, 9, 8B, the subcallosal gyrus, area 25 and the rostral tip of areas 24 had been destroyed on the right side (fig. 1, A, B). On the left side the lesion affected the subcallosal gyrus, the rostral tip of the caudate nucleus, area 13, the rostrum of the corpus callosum and the external capsule ventral to the lentiform nucleus. The Marchi series is of good quality throughout. Degeneration extending rostralward from the lesion tends to show large, coarse fibers, and that at the caudal end of the lesion fine, small caliber of fibers.

Degenerating fibers in the medial portion of the right and left cingulum can be followed from the subcallosal gyri into the cortex of the cingulate gyrus throughout areas 25, 24, 23, 29 and into the isthmus. There appear to be degenerating fibers in the lateral portion of the cingulum which extend into the superior frontal (areas 8B, 9, 6, 4) and parietal (areas 3, 2, 5) convolutions (fig. 5, B). The subcallosal gyri are connected with the cingulate gyrus above the corpus callosum by degenerating fascicles which pass medial to and parallel to the rostrum and over its genu, into the cingulum dorsal to the body of the corpus callosum. Interconnections of the right and left cingulate gyri occur dominantly at the level of the lesion (fig. 5, B). They pass by way of the body and genu of the corpus callosum into the cingulum of the respective convolutions. However, other fibers travel in the cingulum to terminate more caudally in the cingulate gyrus with, or without, decussation in the corpus callosum. There is some evidence to suggest that short fibers extend from area 25 and the subcallosal gyrus through the radiations in the frontal pole rostral to any capsule formation and into the gyrus rectus, areas 12, 13, 45 and 46 (fig. 6, A). This pattern is more conspicuous in the more adjacent cortical laminae of the convolutions.

The right superior frontal lesion connects to the right middle frontal (areas 46 and 8A) and inferior frontal (areas 45, 46 and 6) convolutions, the orbital gyri (areas 12 and 13), gyrus rectus (areas 11 and 14) and the subcallosal gyrus by way of the complex which will separate into the internal, the external and the extreme capsules. Some of the degenerating fibers cross over the genu of the corpus cal-

losum to distribute to the contralateral side. Degenerating fascicles are exchanged between the superior frontal convolution and the cingulate gyrus (figs. 5, A; 6, A). Degeneration granules enter the corona radiata and then the superior longitudinal fasciculus to distribute caudalward from the lesion. Marchi granules are conspicuous in the cortical laminae of the frontal (areas 6 and 4) and parietal (areas 1 and 2) opercula, insula, medial surface of posterior parietal area 5 and the entire inferior parietal convolution (area 7), bilaterally. There are some degeneration granules in the preoccipital gyrus (area 19). It is not possible to rule out whether this pattern includes fibers from the cingulate lesions. Short interconnections appear from the gyrus rectus on the left through the rostrum and genu of the corpus callosum to the gyrus rectus on the right side (fig. 6, A). Interpretation of the evidence does not permit a comparable suggestion regarding the interconnections of area 13.

From the right superior frontal convolution, and probably from the cingulate lesions, degeneration granules in the superior longitudinal fasciculus move ventralward through the postlenticular part of the internal capsule into the inferior fronto-occipital fasciculus to distribute to the superior, middle, inferior temporal and hippocampal gyri. Terminating fibers are prominent along the inferior surface of the superior temporal gyrus and the superior surface of the middle temporal gyrus. A few degeneration granules are evident in the alveus leading toward the hippocampus.

There are some degenerating fibers entering the caudate nucleus bilaterally by way of the subcallosal bundles and the complex from which the anterior limb of the internal capsule will be derived. Putamen on both sides receives degenerating fibers from the anterior limb of the internal capsule and the external capsule. Both pathways contribute to the fibers terminating in the nucleus accumbens bilaterally. The Marchi granules present in right and left globus pallidus have entered the nuclei from the anterior limb and genu of the internal capsule, or have passed directly through the putamen.

Both lateral septal areas receive a substantial quantity of degenerating fascicles. There are some which terminate in the medial septal nuclei. These appear to have come from the lesions above the corpus callosum and to perforate the body of the corpus callosum as the precommissural fornix enters the field, traveling with the latter's fibers into the septal region. On each side, the caudal part of the tuberculum olfactorium with its islands of Calleja is a recipient of a large number of degenerating fascicles which have come through the anterior limb of the internal capsule, and, to a much lesser extent, through the external capsule.

Very slight degeneration in the anterior nuclear group of the dorsal thalamus appears to come by way of the cingulum to the corona radiata, to the anterior thalamic radiations, ventral to the caudate nucleus, through the stratum zonale of the thalamus and into the capsule of the anterior nuclear group (fig. 7). Some fibers seem to pass directly through the capsule and enter the diencephalic periventricular system and the stria medullaris which ends in the habenular nuclei. The medial thalamic nucleus, and particularly the nucleus ventralis anterior on the left side, receive degeneration granules through the inferior thalamic peduncle. Numerous fibers can be observed emerging from the posterior limb of the internal capsule and crossing nuclei ventralis lateralis and ventralis posterior on their way to the red nucleus of the midbrain.

Anterior and lateral hypothalamic areas of both sides receive some degenerating fibers. Part of these travel with the inferior thalamic peduncle (fig. 9, A), and some come with the diencephalic periventricular system (fig. 7). Finally, some have emerged from the cortical components in the position of the ansa and fasciculus lenticularis (figs. 8, C; 9, B, C; 10, A, B).

The fibers of cortical derivation can be seen in the position of both the ansa and fasciculus lenticularis (fig. 9, A, B, C, D), particularly on the left side where the cingulate lesion is also more prominent. Many of these fibers appear to terminate in the nucleus of the field of Forel. Some continue ventrocaudally into the tegmentum of the midbrain (fig. 9, E, F), the interstitial nucleus of the medial longitudinal fasciculus and the nucleus of the oculomotor nerve. In the posterior limb of the internal capsule there are a substantial group of fine, small fibers. They are in contrast to those few fibers of larger caliber destined for the cerebral peduncle as frontocorticopontine tracts. These former degenerating fascicles interweave with the comb bundle as it passes through the cerebral peduncle and terminate in pars compacta and pars reticulata of the substantia nigra (fig. 6, B).

Animal C-S-11, a small male macaque, approximately 2.3 kg, in weight, was operated upon on November 1, 1957. The convex surface of the brain was retracted gently to expose the right posterior cingulate gyrus. Stimulation of the isthmus region produced noisy, labored respirations. A large amount of mucus and saliva collected in the mouth and throat during the procedure, necessitating continued aspiration to maintain a clear airway. As the stimulating electrode was moved forward onto area 23, alternating clonic flexion and extension occurred in the upper (fig. 4, B, C) and lower extremities. These movements included the shoulder, elbow, wrist, and metacarpophalangeal joints in the upper extremity, and, correspondingly, the hip,

knee and ankle, and metatarsophalangeal joints in the lower extremity. Throughout all the region stimulated there were facial movements involving the muscles of facial expression and the muscles of mastication. Thus a grimace was produced. Facial movements were bilateral and homolateral, and the extremity movements were bilateral and contralateral (fig. 4, B, C).

At the completion of the two and one-half hours of surgery the body temperature had dropped 4.5°C. Preoperative rectal temperature was 39.8°C, and postoperative temperature was 35.2°C. There was intense shivering for 30 minutes as the body heat was slowly regained. The animal appeared cyanotic around the face and the body was cold to touch. The character of respirations was shallow, stertorous, dyspneic and slow. Preoperative respiratory rate was 70 times per minute and postoperative rate was 24 per minute. Both pupils appeared dilated at the end of the surgery, with a greater dilatation evident in the left eye. Piloerection was very noticeable (fig. 4, E).

The animal was alternately sleepy and hyperkinetic from the few minutes immediately following surgery to 4 days after the procedure. At one time the monkey would yawn and doze. In the next few minutes the monkey would pace the cage, circle around and around, climb, making attacking movements, rub the face, eyes, and head, or roll the head around upon the neck. The hyperactivity was massive and generalized to the point of an epileptic seizure during the first day following the experiment. Some dysmetria of the face was noticeable and the left side showed weakness in comparison to the right side. The spontaneous contraction of right facial musculature resembled a tic.

This animal was excessively vocal after the surgery. The cry was usually a low-pitched, sustained one with no particular association to the events around the animal. The monkey was aggressive (fig. 4, E) rather than fearful. There was no essential difference in his behavior pattern when he was placed with a cage mate and C-S-11 was equally adept in competition for food.

Examination of the brain at necropsy showed an extensive lesion in the right posterior cingulate region. This included areas 23, 29 and isthmus. Slight compression damage from packing for hemostasis at the operation was evident on the medial surface of the superior parietal lobule. This latter was present in the Marchi preparation with minimal extension into the fiber paths from areas 3 and 2. The Marchi preparation appeared to be a good penetration of the tissue. There were no regions of the cortical laminae into which appreciable terminal degeneration could be followed. There was no difficulty in tracing degenerating fascicles along the white matter, or into the subcortical structures.

From the site of the lesion fibers travel rostrally in the cingulum on both right and left sides. The latter have crossed successively through the body and the genu of the corpus callosum. The position of the degeneration in the cingulum suggests that there are bilateral connections from posterior cingulate to anterior cingulate regions all along the course of the gyrus. A considerable percentage of the degenerated fibers of the cingulum pass over the genu of the corpus callosum and into the region of the right and left subcallosal gyri.

Some of the degenerated fascicles in the cingulum travel out into the medial side of the corona radiata and into superior parietal (areas 3, 2, 5), frontal (areas 4, 6, 8, 9, 10) and pre-occipital (area 19) convolutions (fig. 5, B). These radiations pass to the left side by way of the body of the corpus callosum. The greatest quantity of fibers appear adjacent to the lesion, in the parietal convolution (areas 3, 2, 5). White matter of the middle and inferior frontal (areas 8, 45, 46) and parietal (areas 1, 2) convolutions are receiving degenerated fibers which enter the cingulum, the corona radiata and the external and extreme capsules. Many of the fibers are directed toward parietal and frontal opercular regions (areas 4, 6, 1, 2) and area 13 of the orbital gyri. It was not possible to distinguish fibers entering the insula. Fibers crossing in the body of the corpus callosum followed the pattern of distribution described above for middle and inferior frontal and parietal convolutions. Some degenerated fascicles extend ventralward in the rostrum of the corpus callosum toward the gyrus rectus in the left and the right frontal lobes. These are joined by some fibers from the cingulum traveling the external capsule ventral to putamen and dorsal to orbital gyri.

The white matter of the temporal lobe from its most rostral to caudal extent, including the transition into occipital cortex, is generously supplied bilaterally with degenerated fibers. This encompasses the tracts entering superior, middle and inferior temporal gyri, hippocampal gyrus and hippocampus, bilaterally. The pathway to the rostral temporal regions, excluding the hippocampus, extends from the lesion, to cingulum to corona radiata, to external and extreme capsules and into superior, middle, inferior temporal gyri and hippocampal gyrus. The extreme capsule appears to direct more fibers toward superior and middle temporal gyri, and the external capsule to direct more fibers toward inferior temporal and hippocampal gyrus. The degeneration reaching the caudal portion of the temporal lobe is evident in the cingulum, corona radiata, postlenticular part of the internal capsule, inferior fronto-occipital fasciculus and the subdivisions of the temporal lobe. In both of the pathways described fibers cross in the body of the corpus callosum to reach the left side.

At the most caudal limits of temporal lobe as it continues into occipital cortex, the hippocampus receives fibers by a dual route. From the cingulate gyrus degeneration passes into cingulum, thence to corona radiata, then to the postlenticular limb of the internal capsule and into alveus toward the hippocampus. Some fibers which do not enter alveus extend into inferior and middle temporal convolutions. Fascicles cross in the splenium of the corpus callosum to reach the left side by the above pathway. Some fibers from the cingulum enter the fornix to approach the hippocampus. There are degenerated fascicles in the posterior hippocampal commissure extending into the left fornix also.

It appears by the pattern of degeneration that fibers connect the posterior cingulate region to the caudate nucleus and globus pallidus on both sides. Fibers reach the caudate nucleus by travelling through the cingulum to the corona radiata, then to the subcallosal bundle and the anterior limb of the internal capsule. Fascicles entering the globus pallidus had passed from cingulum to corona radiata and thence to anterior and posterior limbs of the internal capsule in their course.

In the dorsal thalamus the right and left anterior nuclear groups are degenerated. Fibers could be traced by their osmic stain from the cingulum to the corona radiata then by way of the anterior thalamic radiations, and through the stratum zonale into the anterior nuclear group (fig. 7). Crossed fibers are visible in the body of the corpus callosum. The greatest degeneration is in the nucleus anteroventralis. A number of fibers extend from the anterior nuclear group into the diencephalic periventricular system (fig. 7). Some of the terminal degeneration in the anterior and lateral hypothalamic areas appears to have traversed this system.

In the course (fig. 9) of the ansa lenticularis and fasciculus lenticularis there are numerous degenerating fibers with a marked diminution, suggesting synapse, in the nucleus of the field of Forel. Those fibers present in the position of the fasciculus lenticularis had passed from the cingulum to the corona radiata through the posterior limb of the internal capsule and over the dorsal surface of the globus pallidus (fig. 9, A, B). Those fibers present in the position of the ansa lenticularis traverse the external capsule, pass ventral to the lentiform nucleus, and swing dorsalward through the medial segment of the globus pallidus to emerge in the area of the ansa lenticularis (fig. 9, A, B). Some of these fibers go ventralward into the tegmentum ventral and lateral to the red nucleus in the midbrain (fig. 9, E, F). Other fibers from the lesion leave the posterior limb of the internal capsule and extend diffusely through the dorsal thalamic nucleus ventralis lateralis and nucleus ventralis posterior to the red nucleus. These

corticorubral fibers have crossed in the body of the corpus callosum. A number of the degenerated fibers from the lesion which have reached the postlenticular limb of the internal capsule interdigitate with the fibers of the comb bundle to terminate in the pars reticulata and the pars compacta of the substantia nigra (fig. 6, B). A crossed corticonigral component passes over the body of the corpus callosum.

Animal C-S-12, a 2.7 kg female macaque, was operated upon on November 5, 1957. The stimulation was carried out from a caudal to a rostral direction on the right anterior cingulate gyrus. A homolateral facial grimace was produced by the stimulation (fig. 4, B, C). Upper extremity movements of alternate flexion and extension occurred (fig. 4, B, C). As the electrode was moved forward on the cortex the movements of the face persisted with the addition of nystagmus and protrusion of the tongue. The nystagmus was vertical with the quick component upward, then, with more rostral stimulation, horizontal with the quick component ipsilateral. The protraction and retraction of the tongue were also toward the right side. Respiratory and cardiac activity became very irregular as the stimulation was applied to the region of the subcallosal gyrus. Respiration decreased from 72 to 20 times per minute during stimulation. An apnea lasting 30 seconds was produced. After the placing of a lesion in the region stimulated, respirations were irregular and gasping. When a rate was established it was 100 and paradoxical in type. Cardiac irregularity in this same region of stimulation proceeded from 88 to 40 times per minute, to 120, to 50, to 160, as the lesion was placed. The heart rate stabilized at 95 per minute.

At the completion of the surgery the animal's rectal body temperature had dropped 2.0°C from 39.5°C to 37.5°C. The shivering manifested with a body cold to touch persisted for 30 minutes. At the end of this time rectal body temperature measured 39.0°C. The animal was quiet and sleepy. Such drowsiness continued 4 days. Piloerection (fig. 4, E) was apparent upon the completion of the operation. In the postoperative period C-S-12 was hyperkinetic. She circled clockwise for long intervals (5 minutes) without interrupting the pace (20 circuits in 0.5 minute). She would pull at her bandage and rub her face more than other operated animals. It was possible for the examiner to feed her without apparent fear on the part of the animal. There was neither a dominant nor a submissive role assumed by this monkey with her cage mate. She was not vocal or noisy in the conduct of her body movements.

When the brain was removed and examined it was found that the lesion had included areas 24 and 25 on the right side. Grossly there was slight compression damage in the right superior frontal convolu-

tion in areas 8B, 9, 10 and 45. The corpus callosum had no observable lesion, but was friable and tore in the necropsy examination of the brain. Marchi preparation showed impregnation of the corpus callosum, the superior frontal convolution, and the left anterior cingulate gyrus in such a fashion that the material suggests there had been death of this tissue postoperatively from ischemia around the single anterior cerebral artery.

There are coarse Marchi granules from the region of the lesion that travel forward in all the fiber paths to end points in cortical laminae. They are present in greater quantity on the side of the original lesion and extend into areas 8A, 46, 12, 13, 11 and gyrus rectus of both sides and into areas 6, 8B, 9 and 10 of the contralateral frontal cortex. Caudal to the level of the lesion, degeneration granules are present in the right and left superior longitudinal fasciculi. These granules extend into the superior, middle, and inferior frontal (areas 4 and 6), and superior and inferior parietal convolutions (areas 1, 2, 3, 5 and 7), but the granules cannot be traced unequivocally into cortical laminae.

An appreciable number of fibers enter the right and left inferior longitudinal fasciculi and lead bilaterally into superior temporal, middle temporal, inferior temporal, hippocampal gyri and hippocampus. As the degenerating granules come from the lesion into the corona radiata, some will extend into the external capsule and others will pass into the extreme capsule to reach the subdivisions of the temporal lobe. Fibers that have travelled in the cingulum can be observed coming ventralward into the alveus toward the hippocampus (fig. 8, B). Some of these have crossed in the splenium of the corpus callosum. A portion of the fibers in the cingulum enter the fornix with, or without decussation in the posterior hippocampal commissure to reach the hippocampus.

The cingulate gyrus immediately caudal to the lesion has the greatest percentage of cortical degeneration. It involves a very fine calibre of fiber. However, fascicles can be followed in the ventromedial part of the cingulum throughout the full extent of the gyrus into the isthmus region. They are present on both sides, but intrusion of the lesion into the corpus callosum does not permit observation of crossed fibers. There are connections from the right and left cingulate gyri into the respective superior frontal (areas 9, 10, 8, 6, 4) and parietal convolutions (areas 2, 3, 5), and conversely.

Most of the degeneration present in the caudate nucleus is in the head, but fibers can be seen entering the tail also. These fibers have reached the head of caudate nucleus by way of the subcallosal bundles and anterior limb of the internal capsule. A few fascicles in the sub-

lenticular part of the internal capsule pass into the inferior fronto-occipital fasciculus, thence to the tail of the caudate nucleus. Some degeneration is present in the nucleus accumbens and appears to come through the external capsule. There is no apparent degeneration in the putamen. The numerous fibers which reach the globus pallidus have travelled from the lesion through the anterior and posterior limbs of the internal capsule.

Degeneration is present in the lateral and medial septal nuclei, and the tuberculum olfactorium. It is possible that perforating fibers of the precommissural fornix have been interrupted by the infarction in the corpus callosum. The lateral preoptic area is receiving fibers that may also have come with the precommissural fornix looping over and through the anterior commissure as it appears. There is some evidence that the medial forebrain bundle is also bringing a portion of the degenerated fibers to the preoptic area.

In the dorsal thalamus the anterior nuclear group of both sides receives a few degenerated fibers from the cingulate gyri by way of the anterior thalamic radiations, ventral to the caudate nuclei, through the stratum zonale and into the capsule of the anterior nuclear group (fig. 7). Some of the degenerating fibers go on through the capsule of the anterior nuclei into the stria medullaris, ending in the habenular nuclei. Another portion of the fibers extend medialward from the stria medullaris and into the diencephalic periventricular system (fig. 7). Degeneration, which has come by way of the anterior thalamic radiations, can be seen in the right medial nucleus. It is present in both magnocellular and parvocellular parts of the medial nucleus.

There is evidence of degeneration in the anterior hypothalamic areas on both sides. This occurs at the transition of the preoptic area into hypothalamus and appears to be the termination for the fascicles in the medial forebrain bundle. The dorsomedial hypothalamic nuclei and lateral hypothalamic areas also show degeneration from cortical fibers travelling in the inferior thalamic peduncle (fig. 9, A). Some Marchi granules are present in the capsule of the right and left medial and lateral mammillary nuclei, and ventromedial hypothalamic nuclei. These three areas appear to receive cortical fibers transmitted in the ventral peduncle of lateral forebrain bundle as described below (figs. 8, C; 9, C, D; 10, A, B).

As the ventral peduncle of the lateral forebrain bundle forms it is possible to distinguish the components of cortical origin that are entering in both the positions of the ansa and fasciculus lenticularis (fig. 9, A, B). A large proportion of the degeneration in these components disappears in the field of Forel (figs. 8, C; 9, C, D), but some of it can be followed into the tegmentum of the midbrain (fig. 9, E, F),

the medial longitudinal fasciculus and the oculomotor nucleus. There are some cortical fibers which pass out of the posterior limb of the internal capsule and through the dorsal thalamic nuclei ventralis lateralis and ventralis posterior toward the red nuclei and the tegmentum ventral and lateral to it. An appreciable number of fine fibers in the posterior limb of the internal capsule extend ventromedially into the substantia nigra (fig. 6, B), pars compacta and pars reticulata, of both sides. As the cerebral peduncle forms, some of the fibers in the posterior limb of the internal capsule continue into it as frontocorticopontine and corticospinal tracts.

The following group of animals will be considered together since they were not included in the microscopic portion of the study. Postmortem examination confirmed the regions of the cingulate gyrus involved in the acute and chronic phases of the observations made (fig. 2). Animals C-S-3, C-S-4 and C-S-15 were utilized in acute stimulation experiments. Monkeys C-S-1, C-S-2, C-S-5, C-S-13, C-S-14 and C-S-16 are reported for both acute and chronic experimental data, accumulated in two weeks up through three months.

Animal C-S-3 had had previous surgery on the left hemisphere of the cerebral cortex. Left areas 4 and 1 in the face region of cortical control had been ablated, along with the left superior temporal gyrus down to the temporal pole (fig. 1, B). Left anterior cingulate gyrus was stimulated in a caudorostral direction. Stimulation proceeded from the junction of areas 23 and 24 through 25 at the edge of the genu of the corpus callosum. The contralateral lower extremity and the tail were brought into tonic flexion and extension during the first part of the stimulation. Then, contralateral upper extremity movements accrued from the stimulation. Finally, movements of head, neck, ears, eyes and mouth were produced by the stimulation of the cingulate gyrus. As the head and the facial movements became prominent, they resembled the attacking motions seen in an angry or fearful animal.

Animal C-S-4 had had a prior decortication on the left side. The cortex had been removed from frontal, occipital, parietal and insular cortices. Although the temporal pole and some of the middle and the inferior temporal cortex remained, the association tracts of external and extreme capsules, inferior longitudinal fasciculus, anterior commissure, corpus callosum and fornix had been severed. The basal ganglia were intact in the left hemisphere. On the right hemisphere, there were old healed lesions in areas 4, 2, and 1 which govern voluntary somatic muscular movements. The lesions extended into the region controlling the face. Stimulation was directed rostrocaudally on the anterior cingulate gyrus, encompassing areas 25, 24, and the transi-

tion of 24 into 23. Head and neck movements resulted from all the points stimulated. Bilateral upper and lower extremity movements were present and stronger in the contralateral extremities. At the rostral region of stimulation near the genu of the corpus callosum, discrete movements of periorbital, nasal and oral musculature could be elicited by the stimulation.

Animal C-S-15 had had no previous surgery. The cortex of the cingulate gyrus was stimulated on the left side. Then, after sectioning the falx cerebri, the cortex on the right side was stimulated through the entire expanse of the cingulate gyrus that could be exposed without excessive hemorrhage into the operative field. It was necessary to decorticate the superior convolution and the cingulate gyrus on the left to facilitate the exposure. An attempt was made to establish a linear stimulation with points of reference above and below the experimental line. Since this experiment was used as a guide for the collation of the information in all of the experimentation, it will be recounted as observed in a rostrocaudal direction.

Point 1: facial grimace, respiratory changes.

Point 2: facial grimace, marked neck thrust, respiratory changes.

Point 3: bilateral facial movements, contralateral arm moved forward at shoulder and elbow.

Point 4: bilateral facial movements, tongue protruded, arm brought forward, with extremity movements less above and below the line of reference.

Point 5: facial grimace, neck thrust, teeth closed on the tongue, mouth opened, ears pulled backward and upward, some respiratory changes evident in the laryngeal movements.

Point 6: facial movements, neck thrust, ears pulled backward, mouth opened, contralateral arm flexed, hand flexed into a fist.

Point 7: facial grimace, ears back, mouth opened, neck thrust, contralateral upper extremity movements. Above the line of reference facial movements were less, and upper extremity movements become bilateral. Below the linear point some lower extremity movements began to appear.

Point 8: bilateral facial movements, neck thrust, ears back, clonic movements of upper and lower extremities. Extremity movements were more pronounced at the depth of the gyrus.

Point 9: facial movements, clonic movements of extremities.

Point 10: facial grimace, neck thrust, no lower extremity or abdominal movements.

Point 11: facial grimace, neck thrust.

Point 12: facial movements.

Animal C-S-1 was operated upon on July 5, 1957 and July 20, 1957. Cortex over areas 6, 8B and 9 were ablated in order to reach the cingulate gyrus for stimulation on the left side on the first date, and the right side on the second date. In both instances the stimulation was performed in a rostrocaudal direction on area 24. At all the 5 areas stimulated on each side, there were facial musculature movements. The eyes tended to close with the stimulation. Respiration was slow and irregular during the stimulation. When the stimulation neared the junction of areas 23 and 24, upper and lower extremity movements were present. During the stimulation of the right cingulate gyrus the head moved upward (fig. 4, D), toward the contralateral side and then downward in that order. As the current was elevated to 7 to 10 volts strengths, a generalized convulsive seizure resulted coincident with stimulation of the cingulate gyrus. During the postoperative observations on C-S-1 a piloerection (fig. 4, E) was noted that persisted to sacrifice. Shivering was present after the first experiment. An increased sudomotor response was found when the animal was tested with quinizerine powder. Although there was a transient tendency to sleep right after the first operation, the animal's behavior was essentially one of hyperactivity accompanied by angry, high-pitched vocalization (fig. 4, E).

Animal C-S-2 was operated upon on July 12, 1957 and July 26, 1957. The cortex of areas 6, 8B, 9 and 10 were removed on the left to expose the anterior cingulate gyrus. On the right side comparable cortical areas were denuded. Necropsy showed an atrophic region on the cortex of areas 5 and 7 bilaterally along with a healed surgical lesion in the posterior vermis and posterior lobe of the right hemisphere of the cerebellum. During the stimulation of the left cingulate gyrus near the genu of the corpus callosum, bilateral facial movements were obtained (fig. 4, D). The head was brought up and backward, then turned homolaterally and then directed downward. Movements of the eyes matched those of the head (fig. 4, D). Respirations became paradoxical with prolonged periods of apnea and marked cyanosis about the face. A marked sialorrhea occurred during and following the stimulation. Cardiac irregularity was coincident with the changes in the respiratory cycle. During the excitation of the right cingulate gyrus above the body of the corpus callosum, facial movements occurred by which the eyes were opened. The lower extremity movements appeared homolaterally and then bilaterally. There was piloerection (fig. 4, E) present by the 11th postoperative day. This persisted until sacrifice. Following the first procedure, the monkey was apraxic on the right side. After the second procedure a diplegia appeared accompanied by an intention tremor in the right

upper and lower extremities. While the animal recognized gross tactile stimulation, there seemed to be a blunting of proprioceptive and pain sensations in the lower extremities. Consequently, the feet were often cut and bleeding from hanging and climbing in the cage.

Animal C-S-5 was operated upon on October 24, 1957. Areas 6, 8B and 9 on the left were destroyed to expose the right anterior cingulate gyrus. Areas 24 and 25 were stimulated in a caudorostral direction. Facial movements were bilateral (fig. 4, D) until the cortex rostral to the genu of the corpus callosum was stimulated, and it produced homolateral (fig. 4, B, C) facial contraction. These latter movements included closure of the eye, retraction of the upper and lower lip and closure of the jaw. At the caudal portion of area 24, bilateral movements of the upper extremity resulted from the stimulation. These were a gross flexion at the shoulder, the elbow, the wrist and an internal rotation of the hand. Postoperatively the animal was cold to touch and shivered about 10 minutes. A facial weakness on the side of the lesion persisted to produce a disproportion of the face. Hyperkinesia included pacing, circling and climbing. Vocalization was not greater than that of unoperated animals.

Animal C-S-13 was operated upon on November 8, 1957 and December 6, 1957. On both dates the posterior cingulate region was exposed by gentle retraction of the superior parietal convolution (fig. 2, B). Stimulation of area 23 resulted in facial movements coupled with tonic flexion and extension of the upper extremity (fig. 4, B, C). At the termination of both procedures body temperature had dropped 2.3°C and 1.9°C respectively. Shivering was sustained both times for about 40 minutes. Marked sialorrhea, and pupillary dilatation (fig. 4, D) were present. Vasodilation gave a dusty blue pallor to the face that persisted about three days after each experiment. There was a transient tendency to be sleepy. Respirations were labored, shallow and rapid. Heart beat was very rapid and strong. A postoperative hyperkinesia included gyrations of the head and neck, rubbing of the face, excessive grooming, pacing and circling. A low-pitched vocalization accompanied the activity. This animal did not assume a dominant or submissive role with her cage mate. The observation period extended throughout three months with daily notations. At necropsy (fig. 2, B) there were surgical lesions in areas 23, 29 and isthmus of both sides, and some compression damage from edema was evident bilaterally over areas 3, 2, 5 and 19.

Animal C-S-14 (fig. 2, A) was operated upon on December 10, 1957. After retraction of the superior frontal convolution, area 24 above the body of the corpus callosum was stimulated. Facial movements were produced. These tended to be homolateral at a rostral and inferior
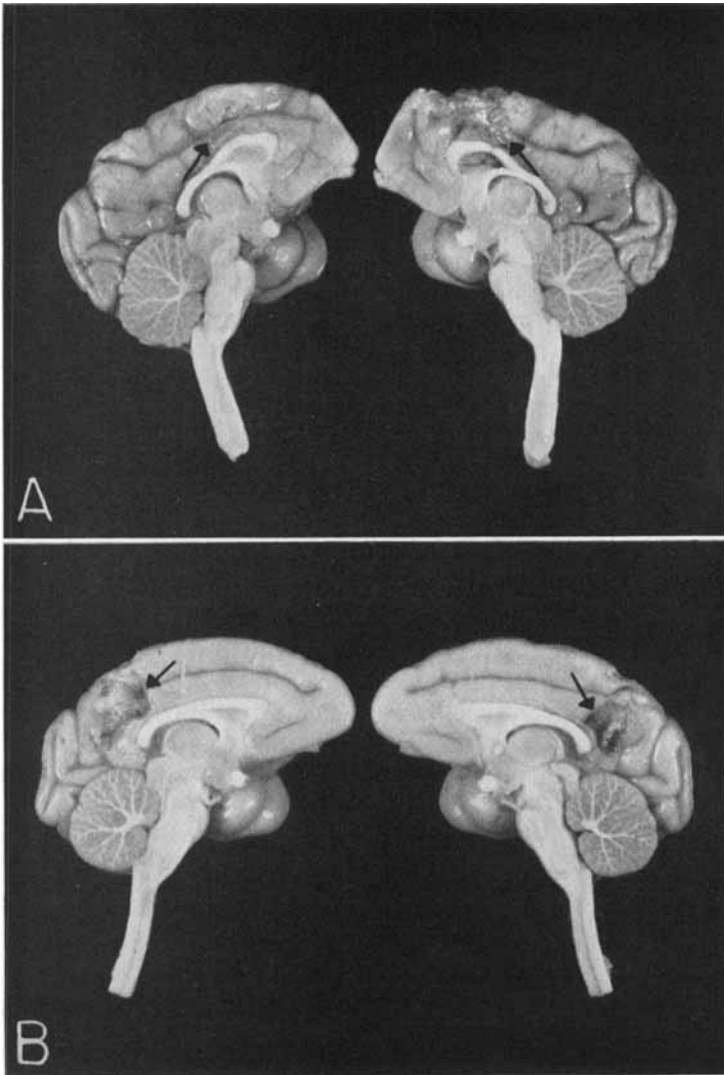
Fig. 2   A, Photograph of the right and left medial surfaces of the brain of C-S-14. Arrows indicate the lesions in the anterior cingulate gyrus (area 24). There is some compression damage from postoperative edema in areas 8, 9, 10. This animal was observed daily for two months. × 0.5. B, Photograph of the brain of C-S-13 showing the right and left medial surfaces of the brain. Arrows indicate the lesions in the posterior cingulate gyrus (areas 23, 29, and isthmus). There is some compression damage from postoperative edema in areas 3, 2, 5 and 19. This animal was observed daily for three months. × 0.5.

position on area 24, and bilateral at a caudal and superior position on area 24. The falx cerebri was divided to reach the left area 24. Stimulation there elicited the same type of facial movements. The cortex above the cingulate gyrus was stimulated on the right and left sides also. This stimulation did not result in any movement of the facial musculature. The cingulate regions stimulated were destroyed bilaterally. Postoperatively, the pupils of both eyes were widely dilated with the greatest dilatation on the side of the last cingulate destruction. This greater pupillary size, in comparison to other animals in the same room, was observed for 10 days. The animal shivered intensely and had a 2.8°C drop in body temperature. Respirations were stertorous, shallow and regular. A regular cardiac irregularity consisting of a stronger third pulsation was noted. Piloerection was present. This monkey was hyperkinetic and vocal during the two months of daily observations. The drowsiness seen postoperatively disappeared in three days. Motor activity was very noisy and the animal appeared to become "angry" at the examiner (fig. 4, E). This was displayed by incessant vocalization of a scolding nature during which the face became bluish-red from vasodilation, pupils of the eyes dilated, head was thrust forward, teeth bared and the cage bars rattled. This animal did not assume a dominant or submissive role with his cage mate. Necropsy examination (fig. 2, A) showed some compression damage from edema to areas 8B, 9 and 10 along with the bilateral anterior cingulate lesions.

Animal C-S-16 was operated upon on February 11, 1958. At this time the left area 8B and 6 were ablated to reach and divide the falx cerebri. Small lesions were placed in the supracallosal area 24 on the left and the right sides. Stimulation of area 24 antecedent to the lesion produced movements of the face, head and neck at the regions sampled just caudal to the genu of the corpus callosum. The movements were essentially homolateral (fig. 4, B, C) and involved muscles of facial expression and mastication. Respiration became stertorous during the stimulation. When the larynx was checked with laryngoscopy, the glottis was closed as the respirations slowed and progressed into apnea. An increase in mucous secretion was noticeable in the nose, mouth and throat. Suctioning was necessary during the rest of the procedure to maintain a clear airway. There was not an increase in salivation. Postoperatively, rectal body temperature had dropped to 36.1°C. This animal shivered approximately 30 minutes. Pupils of the eyes dilated bilaterally. Respirations were rapid, shallow, and stertorous. There was a considerable quantity of mucus present in the throat. Head and neck gyrations occurred. Some increase in the tonus could be demonstrated in the right upper and lower extremities.

Piloerection (fig. 4, D) was evident. In the daily postoperative observations, the animal was hyperkinetic and alternately sleepy. Yawning occurred up to 15 days postoperatively. This animal was a small male who had not been dominant in the colony. During the postoperative period he was placed with a large female who had previously dominated the cage mate behavior with two large male monkeys. C-S-16 was neither dominant nor submissive in this situation. When approached by the examiner, the animal presented an appearance of anger with the following factors noted: (a) piloerection more pronounced, (b) vasodilation with face a dusty blue hue, (c) pupillary dilation, bilateral and more marked on the left, (d) dysmetric face, drooping on the left, tongue deviated to the left, (e) neck thrust forward, (f) mouth opened, lips retracted, teeth bared, (g) eyes wide open, (h) ears drawn backward, (i) no vocalization, but movements for it were present, (j) pacing, circling clockwise, climbing (k) grooming, (l) tending to tremble, (m) yawning intermittently. There was an increase in sudoriferous activity. In addition to this behavior pattern, the animal was curious about his environment.

Somatic experimental phenomena

From the analysis of the results obtained by the stimulation of the cingulate gyrus in 15 animals it is possible to state that a dual pattern of gross somatic movements can be elicited from this cortical region (Showers and Crosby, '58). The anterior portion of the gyrus appears to represent face, head, neck, upper extremities, thorax, abdomen, lower extremities and tail in that order in a rostral to a caudal direction. In the posterior portion of the gyrus this sequence of somatic representation was reversed. The tail and lower extremities, abdomen, chest, upper extremities, neck, head and face are the arrangement depicted by the results obtained. It should be noted that the motor responses of the face were obtained regardless of the region of the gyrus which was electrically excited. These results are illustrated in the diagram in figure 4, A.

All of the somatic movements tended to be gross, such as those which have characterized previous workers' descriptions of additional motor areas. A summary of this work can be found in Crosby ('56). Alternate flexion and extension of

the upper and lower extremities with internal rotation of the part involved was typical of the movements observed. There were discrete movements of the articulations at the shoulder, elbow, wrist, and metacarpophalangeal joints. These were similar to the alterations of position observed at the hip, knee, ankle, and metatarsophalangeal articulations. As the stimulation was applied at the beginning and the end of the regions causing extremity mobility, the initial and terminal movements were at the shoulder and hip joints. Movements of the tail were essentially upward and downward, or flexion and extension in relation to the remainder of the vertebral column. Alternate contraction and relaxation of the abdominal musculature was intensified by stimulation in the middle portion of the cingulate gyrus. These movements altered respiration in terms of increased depth, but did not change the basic preoperative rhythmic pattern of the particular animal tested. Stimulation of the dorsal portion of the appropriate part of the cingulate gyrus tended to produce bilateral upper or lower extremity movements. As the stimulation was applied to the ventral surface of the gyrus the extremity movements were essentially contralateral ones (fig. 4, B, C).

All of the responses included facial movements which possessed characteristics of emotional expression seen in the non-experimental portion of the animal colony. Most of the phenomena observed could be interpreted as parts of anger and attack, or fear and flight. As stimulation was applied to the dorsal surface of the gyrus the facial movements tended to be bilateral, whereas excitation of the ventral surface of the gyrus evoked facial movements, essentially homolateral in nature (fig. 4, B, C). The lips were retracted to bare the teeth, the nostrils dilated, the eyes opened and closed, the jaws opened and closed and the ears pulled backward and upward (fig. 4, D). At the most rostral and the most caudal parts of the cingulate gyrus such somatic responses were seen to the exclusion of motion in the other parts of the body (fig. 4, A). Similar to the somatomotor pattern of the remainder of the body, the sequence of movement of the head and neck was also

reversed in its order. The mouth and the jaws opened and the head was directed downward and forward with stimulation at, or below, the genu of the corpus callosum. The mouth and the jaws opened and the head was directed upward and backward as the stimulation shifted to, or above, the genu of the corpus callosum. The position of the eyes followed the position of the head, although there was a tendency for the lids to close with the upward or downward movement of the head. During the stimulation of the intervening portion of the cingulate gyrus, the head and the neck were directed forward in line with the body by a forcible thrust of the cervical musculature.

In the course of acute phases of the experimentation, the cortical areas adjacent to the cingulate gyrus were explored with the same parameters of stimulation. There were no movements of the body produced which were identical with those from the cingulate gyrus. The superior convolution (protocols C-S-1 through 16) was sampled throughout most of its extent to compare responses from cortical areas 9, 8, 6, 4, 3, 2 and 5 with that of the cingulate gyrus ventral to the specific region involved. Protocols 1, 2 and 16 will show that when the adjacent cortical areas were removed there was no change in the pattern produced. Protocols C-S-11, 12, 13, 14 demonstrate that this pattern was present when the cortical areas bordering the cingulate gyrus stimulated were ablated. The pattern was unchanged by removal of the contralateral supplementary areas (protocols C-S-5, 6, 7, 8, 9). In the acute stimulation of animal C-S-3, the primary motor control area for the face had previously been ablated, and there was no alteration in the pattern elicited by stimulation of the cingulate gyrus on the side of that ablation. Animal C-S-4 had had a prior hemidecortication on the left which had removed both primary and secondary motor areas, and a previous ablation on the right which had included the voluntary motor controls for upper and lower extremities and some for the face. Acute stimulation of the right cingulate gyrus produced results which collated with the others observed. In the elicitation of the parts of the pattern of somatic movements which has been

recounted, the cerebral cortex of all of the animals was excitable with strengths of current ranging from 4 volts to 7 volts. When strengths of current in 7 volts to 10 volts range were applied to the cingulate gyrus, the somatic movements blended into a generalized convulsive seizure (protocols C-S-1, 6).

After destruction of the cingulate gyrus there was a noticeable increase in the motor activity of all of the animals. It was, however, accompanied by an initial and transient tendency to sleep. These animals presented an immediate postoperative picture of alternating extremes of activity, or inactivity. The average drowsiness in 12 animals observed was of three days duration. This ranged from no signs at all in one animal (C-S-6) to 13 days of sleepiness in another animal (C-S-8). The most pronounced tendency to sleep occurred when large lesions were placed in the supracallosal portion (C-S-2, 8, 16) of the cingulate gyrus in the region where excitation gave the greatest variety of somatic movements (fig. 4, A). Lesions in the posterior part (C-S-6, 7, 11, 13) of the gyrus were associated with about 4 days' inclination to be drowsy, and those in the anterior part (C-S-9, 12, 14, 16) of the gyrus had an average of about two days' sleepiness. The rostral and caudal parts of the gyrus were also those from which the least variety of somatic movements was obtained. The hyperkinesia included a multiplicity of movements that appeared compulsive. The animals would climb up and down and around in their cages, repeating over and over the same directions in their paths. There were gyrations of the head and neck. Two animals groomed their fur for prolonged periods. Pacing and circling movements were common. Frequent rubbing of the face and the head were present in most of the animals. In 8 animals the motor activity was noisy and in the 4 others it was not. In C-S-11 the hyperactivity was intense enough to typify a generalized convulsive seizure.

Most of these animals were curious about their surroundings. Three did not display any particular fear of the exam-

iner postoperatively and their motor activity was quieter. Nine animals manifested aggressive movements toward the examiner, but these were not greater than in unoperated animals. The animals showing attacking movements tended to be noisy also (fig. 4, E). There was not a dominant or a submissive role shown in the experimental animals. Two (C-S-13, 14) were tried as cage mates before and after cingulectomy (fig. 2). One small male (C-S-16) was tried as a cage mate with a large female who had been previously dominant of two large male animals. There was some indifference in the conduct of the cingulectomized animal toward its cage mate.

In the immediate postoperative observations, 5 animals demonstrated a noticeable deviation of head, neck, eyes and tongue toward the side of the cingulate lesions (C-S-2, 4, 7, 8, 11). A dysmetric face, in which the weakness occurred on the side of the face ipsilateral to the lesion, was present during the period of observation in three animals (C-S-6, 8, 9). These animals had ablations in some contralateral additional motor areas. In animal C-S-11, in which there was very slight right additional motor area destruction along with a substantial right cingulate lesion, the homolateral part of the face contracted spasmodically. A number of animals (C-S-1, 2, 4, 6, 7, 8, 9, 11) were disinclined to use upper and, or, lower extremities during the period of chronic experimentation. In all of these animals there had been destruction of supplementary motor cortices contralateral to the affected extremities, and cingulate lesions homolateral to the affected extremities. In animal C-S-11, mentioned above, bilateral lower extremity dysmetria was present. The stimulation and destruction had included the region manifesting bilateral lower extremity movements also. In animal C-S-6, bilateral lower extremity weakness was associated with bilateral lesions in the superior frontoparietal convolution and minimal destruction in the cingulate cortex. There was not a significant change in the general muscular tonicity at any time in the experimentation.

Visceral experimental phenomena

A series of autonomic responses occurred simultaneously with the somatic phenomena that have been described as resulting from the stimulation of the cingulate gyrus. Essentially these were confined to the most rostral and the most caudal expanses of the convolution. They were obtained in the subcallosal and isthmus regions where somatic movements were dominantly those affecting the musculature of the head and the neck.

Cardiovascular alterations were noted (C-S-2, 11, 12, 13, 14). Heart beat became alternately very rapid and weak (120–160 times per minute), or very slow and strong (40–50 times per minute). This rate contrasts with a strong, regular, average pulse rate of 88 beats per minute. Occasionally, the cardiac irregularities (C-S-12, 13, 14) were sustained for about 30 minutes after the operative procedure. During this same period all of the animals were cyanotic around the face and buccal mucosa. The pale, blue color was associated with a low body temperature. In animals where lesions were essentially in these regions yielding vasomotor alterations, some showed prolonged effects of the changes (C-S-2, 13, 14). Along with noisy activity the skin of the face became a bluish-red color.

Respiratory irregularities (C-S-1, 2, 9, 11, 12, 13, 15) were concomitant with cardiovascular changes. The respiratory cycle varied from rapid and shallow to slow and deep (100–20 times per minute). The average respiratory rate in the normal animal is 36 respirations per minute. As the cycle became slower, respirations were more labored. Vocalization occurred with forced expiration. It was possible to arrest respiration completely for 30 seconds. When some animals were checked by laryngoscope (C-S-15, 16), it was found that the glottis closed as apnea was produced by the stimulation.

An increase in salivary and mucous secretions also accompanied the stimulation in these parts of the cingulate gyrus (C-S-2, 9, 13). It was possible to distinguish sialorrhea from

increased mucous secretion. The latter was more pronounced as more profound changes in respiration occurred (C-S-16).

A marked drop in body temperature occurred in the majority of the animals in which destruction of the cingulate gyrus was carried out. This drop ranged from 1.8°C up to 4.7°C and averaged 3.0°C in the 9 animals followed (C-S-5, 6, 7, 8, 9, 11, 13, 14, 16). Body heat was elevated in about 40 to 60 minutes. During the phase of returning body heat the animal shivered intensely for the same span of time. Movements resembling shivering were noted in two animals (C-S-9, 16) during the chronic phase of the experimentation. There was an increase in sudomotor activity as compared to the preoperative state (C-S-1, 11, 12, 16). The relative amount of perspiration was evaluated by application of quinizerine powder to palmar, plantar and alar surfaces of hands, feet, and face, after initial cleansing and drying. Piloerection was present in all of the animals as the operation was completed (fig. 4, E). This was evident to the date of sacrifice and it became intensified in a positive correlation to the hyperkinesia and general excitation of the animal.

Stimulation and destruction of the rostral and caudal portions of the cingulate gyrus caused a dilation of the pupils of the eyes (C-S-6, 7, 8, 13, 14, 16). This was most apparent in the pupil of the eye contralateral to the cingulate cortex ablated (fig. 4, D). The pupillary dilatation was present from a few hours up to 7 days postoperatively. It was noted in some of the noisier animals that the pupils of the eyes increased in size as the emotional and somatic activity became more intense.

Vocalization was a prominent feature in the behavior pattern of these animals after surgery. Eight out of 12 were conspicuously noisy. One animal (C-S-16) went through all the motions of sound production without voice. A preoperative notation had not been made on this point. Only three animals (C-S-2, 5, 12) were quieter in comparison to their preoperative state. The vocal sounds resembled those of a shrewish, high-pitched, angry complaint, or a low-pitched, detached call. The

former was directed at the examiner, or animals in the colony. The latter had no apparent association with the surroundings. In the first instance (C-S-1, 8, 9, 14), there were lesions in the anterior cingulate gyrus. In the second instance (C-S-7, 11, 13), there were lesions in the posterior cingulate gyrus. It has been mentioned that noisy aggressive movements were present in most of the animals. It seems appropriate to call attention collectively to movements belonging to the facies and to associate them with the signs of emotional expression: piloerection, vasodilation, pupillary dilatation, eyes widely opened, neck thrust forward, mouth opened, lips retracted, teeth bared, jaws parted, ears drawn backward, tremor in the head and neck, and vocalization.

Afferent connections of the cingulate gyrus

The anatomical connections of the cingulate gyrus have not been worked out in any great detail. The investigators are agreed that the anterior nuclear group of the dorsal thalamus projects to the cingulate gyrus (Meyer, Beck and McLardy, '47; Ward, '48; Rose and Woolsey, '48; Pribram, Lennox and Dunsmore, '49; Kaada, Pribram and Epstein, '49). Many of these workers are presenting data based upon strychnine neuronography. The greatest specificity is described by Rose and Woolsey ('48) and Meyer, Beck and McLardy ('47). Rose and Woolsey, in discussing rabbit and cat indicate that the projection of the anteromedial nucleus is to the anterior limbic area; the anteroventral nucleus to the cingular field, and the anterodorsal nucleus to the retrosplenial area. Meyer, Beck and McLardy, in an analysis of material prepared from leukotomized humans, state that the anteromedial nucleus projects to the precallosal part of the cingulate gyrus and to the posterior cingulate gyrus in an axial orientation. The present study does not contribute any information about the subcortical projections to the cingulate gyrus.

Other afferent connections are described by Bailey, von Bonin et al. ('44) by using strychnine neuronography. This

technique indicated that the suppressor areas 24s, 8s, 4s, 2s, and 19s project to a cingular belt, along the sulcus cinguli. Using this same technique Pribram, Lennox and Dunsmore ('49) describe corticocortical interrelationships for the trigonal, subcallosal, medial orbital, precallosal, cingulate, posterior orbital and anterior insular areas. McLean and Pribram ('53) relate the medial parieto-occipital region to posterior cingulate, the medial frontoparietal to rostral cingulate and the medial frontal to subcallosal areas by neuronographic methods applied to the macaque monkey. Mettler ('35)
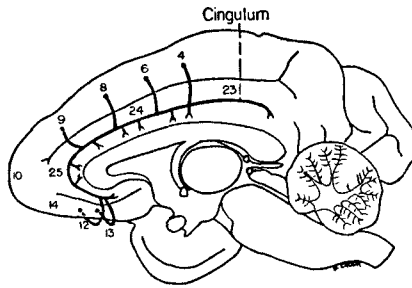

Fig. 3   Diagram of frontocingulate pathways.

claimed that areas 6 and 9 were connected to the cingular and subcallosal gyri and that area 17 projected to posterior cingulate gyrus up to the level of the paracentral lobule. Glees et al. ('50) stated that areas 4, 6, 8, 9, 10 are connected to the anterior cingulate region. Showers ('58) describes projections from frontal cortical areas 8, 9, 12, 13 and 4 into the cingulate gyrus, especially to the anterior cingulate region (fig. 3). The present work supports that previously done relevant to area 4 (protocols 6, 8), area 6 (protocols 8, 12), area 13 (protocol 9), area 9 (protocols 9, 12) and area 8 (protocols 8, 9, 11). There is evidence that area 10 (protocols 9, 12) and areas 3 and 2 (protocols 6, 7, 11) are also contributing short, comparatively direct association fibers to the cingulate gyrus.

Efferent connections of the cingulate gyrus

Most of the investigators present the efferent connections of the cingulate gyrus from studies based upon strychnine neuronography. Bailey, von Bonin et al. ('44) state that area 29 connects to the anterior nucleus of the thalamus. Pribram and Fulton ('54) found the subcallosal area to connect to medial and ventral parts of the anteromedial nucleus and the nucleus parataenialis of the dorsal thalamus; anterior cingulate part connecting to a strip between nuclei anteromedialis and anteroventralis; posterior cingulate connecting to nucleus anteroventralis. Murphy and Gellhorn ('45) showed the prefrontal, motor, sensory and cingulate cortices discharging to the dorsomedial nucleus of the thalamus. Dunsmore and Lennox ('50) related the supracallosal parts of the anterior cingulate area to areas 31, 32, 6s, 4s and possibly to 8s, 2s, and 19s. Pribram, Lennox and Dunsmore ('49) found interconnections in trigonal, subcallosal, insular, temporopolar, periamygdaloid and entorhinal areas.

Glees silver method and Marchi technique have yielded some information in regard to efferent connections of the cingulate gyrus. Gardner and Fox ('48) found that the cingulum degenerated occipitalwards after interruption in the region of area 24. Some of the fibers entered areas 18 and 19. Most of the fibers entered the subiculum and approximated the hippocampus. Smith ('45) could find no evidence for existence of pathways from the rostral cingulate gyrus to the hypothalamus. Ward ('48) followed Marchi granules in the cingulum to areas 31, 18, 19, precentral and postcentral gyri. He did not locate degeneration in the caudate nucleus, putamen, or globus pallidus; hypothalamus or thalamus. He did find degeneration in the lateral septal nuclei, medial longitudinal fasciculus and reticular formation at pontine level. Kaada, Jansen and Anderson ('53) indicated that the cingulum connects to the hippocampus by way of subiculum and presubiculum. By use of silver methods Glees et al. ('50) suggested that the connections from anterior area 24 were intracortical and those from

posterior 24 and 23 were thalamic. These workers felt that the cingulum was more related to the anterior perforated space, than to the cingulate gyrus. Adey ('51), using the Glees method on rabbit, associated the posterior cingulate area with subiculum and presubiculum having commissural connections in the corpus callosum. He stated that the anterior cingulate gyrus connected to the posterior cingulate areas by fibers which terminated in laminae I and IV.

Intercortical connections

In the present study, the efferent connections of the cingulate cortex will be discussed as intercortical and subcortical pathways. The cingulate gyrus of one side appeared to connect to its contralateral gyrus by way of cingulum, to genu and body of the corpus callosum, to cingulum and into cingulate gyrus (protocols 6, 7, 8, 9, 11, 12). These fibers are travelling medially in the cingulum. Since the greatest degeneration was at, or caudal to, the lesion, it suggests that many of these are short, direct connections. An exception occurs in respect to the subcallosal gyrus (protocols 6, 7, 11) which projects all the way back to the isthmus region and conversely (protocols 9, 12). This supports Mettler's ('35) concept that fibers are travelling in both directions in the cingulum. These were dominantly uncrossed intracingulate pathways, along with multiple intercingulate association fibers.

Short, relatively direct tracts brought the efferent fibers of cingulate gyrus into association with the superior frontal and parietal convolutions (fig. 5). These were conspicuous at the level of a cingulate lesion. The cingulate connections with the superior frontal convolution could be followed into areas 4, 6, 8, 9 and 10 (protocols 6, 7, 8, 9, 11, 12). The cingulate connections with superior parietal convolution could be followed into areas 2, 3, 5 (protocols 6, 7, 8, 9, 11, 12). These cingulofrontal and cinguloparietal tracts occupy a lateral and dorsal position in the cingulum and swing across the medial edge of the corona radiata to ascend medially in the radiation path up to the superior convolution.

Interpretation of the microscopic evidence suggests that the cingulate gyrus follows the pattern of frontal intercortical associations to the middle and inferior frontal convolution, inferior parietal convolution, and temporal lobe that has been observed before (Showers, '58). The pathway for frontal and parietal radiations was from cingulum into corona radiata to superior longitudinal fasciculus and into the dorsal surface of the complex that separates to form internal, external and extreme capsules, and thence to the convolution in question. These were dominantly homolateral connections and included areas 8A and 46 in middle frontal region; 45, 46, 4 and 6 in inferior frontal convolution, and areas 11, 12, 13, 14 on the orbital surface (protocols 6, 7, 8, 9, 11, 12). In the inferior parietal convolution, areas 1, 2, 5 and 7, and preoccipital area 19 were involved (protocols 6, 7, 8, 9, 11, 12). Although the evidence is not conclusive, it seems desirable to include a reference to this pathway also leading into the insula, particularly when the Marchi granules are apparent in the opercula of frontal and parietal cortices (protocol 9).

To the temporal lobe, as in the instance of the frontal, parietal and insular degeneration, the adjacent superior cortical areas contributed their fascicles along with those from the cingulate gyrus. This involved superior, middle, inferior temporal and hippocampal gyri. Several methods of distribution in the temporal lobe were observed. These could be interpreted as appearing along a vertically oriented axis that would allow the most direct passage of the fibers. The paths will be presented in their rostral to caudal orientation. From the cingulate gyrus, the fibers enter the cingulum, corona radiata, superior longitudinal fasciculus and then the capsule complex. As this complex separates into external, extreme and internal capsules, those fibers terminating in the superior and middle temporal gyri follow the extreme capsule, and those ending in the inferior and hippocampal gyri follow the external capsule (protocols 6, 7, 8, 11, 12). Some of the fibers in the external capsule decussated through the anterior commissure (protocols 6, 7, 8). Many fascicles entered the inferior longi-

tudinal fasciculus (protocols 6, 7, 8, 12) before their distribution throughout the temporal lobe. Other fibers which have entered the cingulum and corona radiata then go on to the postlenticular limb of the internal capsule, inferior fronto-occipital fasciculus and the radiations leading to the subdivisions of the temporal lobe (protocols 9, 11). As the tracts travel toward hippocampal gyrus some fibers enter the alveus (protocols 7, 8, 9, 11, 12). In the posterior cingulate region as the cingulum turns ventralward in the field, its component fibers can also be observed in their pathway to the alveus (protocols 8, 11, 12). This agrees with the description of afferent fibers to the hippocampus in the cingulum (Kaada, Jansen and Anderson, '53). From this same posterior cingulate region fibers from the cingulum perforate the splenium of the corpus callosum and enter the fornix, with, or without, decussation in the posterior hippocampal commissure to reach the hippocampus (protocols 7, 8, 11).

Subcortical connections

In a comparison of protocols 6 and 11 and by reference to earlier work (Showers, '58), it appears that the discharge of the cingulate gyrus to the basal ganglia is essentially to globus pallidus, and, to a lesser extent, to the caudate nucleus. Fibers from the cingulate gyrus do not appear to reach putamen, nucleus accumbens, amygdala and claustrum. The pathways to the caudate nucleus are from the cingulum to the corona radiata, and dorsally by way of the subcallosal bundle, and/or ventrally by way of the anterior limb of the internal capsule. Those fibers terminating in the globus pallidus appear to reach it principally by way of the cingulum to the corona radiata, thence through the anterior and posterior limbs of the internal capsule.

The anterior nuclear group of the thalamus receives some fibers from the cingulate gyrus (protocols 6, 7, 8, 9, 11, 12). The pathway (fig. 7) of these fibers is from cingulum to the corona radiata, then through the anterior thalamic radiations into a position ventral to the caudate nucleus and dorsal to

the posterior limb of the internal capsule, and over the stratum zonale into the anterior nuclear group. It could be followed in all of the series examined. The greatest quantity of degeneration was in the nucleus anteroventralis, and it was more evident with lesions in the supracallosal portion of the cingulate gyrus at the transition of areas 24 and 23 (protocol 8).

In the hypothalamus, the cingulate gyrus appeared to contribute fibers to the anterior, lateral and posterior hypothalamic areas consistently (protocols 6, 7, 8, 9, 11, 12). Part of the very finely medullated fascicles came by way of the diencephalic periventricular system (protocols 6, 7, 8, 9, 11, 12), and others travelled with the inferior thalamic peduncle (protocols 9, 12). A third group travelled in ventral peduncle of the lateral forebrain bundle (protocols 6, 8, 9, 12). This ventral peduncle includes the ansa lenticularis and fasciculus lenticularis. Portions of these routes are shown in figures 7; 8, C; 9, A-D.

Direct corticotegmental paths, to which the cingulate gyrus contributes, follow two general routes. Those which traverse the position of the ventral peduncle of the lateral forebrain bundle are described in all of the protocols (fig. 9). From the cingulate gyrus fibers enter the cingulum, corona radiata, external capsule, ansa lenticularis in that order and then swing dorsomedial through the medial division of globus pallidus. There they meet comparable fibers which have come through cingulum, corona radiata, and posterior limb of the internal capsule into the dorsal portion of medial segment of globus pallidus. The two groups of fibers follow the position of the lenticular fasciculus into the field of Forel (fig. 9, C, D). After an appreciable synapse in the nucleus of the field of Forel, some fibers pass caudalward to the tegmentum (fig. 9, E, F) ventral and lateral to the red nucleus in the midbrain. The other general route followed by the corticotegmental fibers is traced from the cingulum to corona radiata into the posterior limb of the internal capsule and usually across the nucleus ventralis lateralis and nucleus ventralis posterior of the dorsal thalamus interdigitating with the upswinging fibers of the

medial lemniscus. These fibers also can be followed into the ventral and the lateral tegmental areas (protocols 8, 9, 11, 12). The evidence suggests that some of the corticotegmental paths extend into the medial longitudinal fasciculus and oculomotor nucleus (protocols 5, 7, 8, 9, 12).

A corticonigral path, which includes the contribution of the cingulate gyrus, traverses the cingulum to corona radiata into the postlenticular part of the internal capsule. There, as the cerebral peduncle forms, the fibers mingle with those of the comb bundle and terminate in the pars compacta and the pars reticulata of the substantia nigra (fig. 6, B). This is a crossed and uncrossed path (protocols 7, 8, 9, 11, 12).

Neuroanatomical implications of experimental results

Somatic phenomena

It has already been commented upon that the nature of the somatic movements found in this study is essentially identical with those described by other workers (see p. 260) as characteristic of the type obtained from additional motor areas. Some of these same somatomotor changes were obtained by Sloan and Kaada ('53) by stimulation of the anterior cingulate region. On the basis of the microscopic evidence the cingulate gyrus appears to contribute substantially to the direct corticotegmental paths, and, to a lesser degree, to the corticorubral paths. These tracts permit synaptic relay from the tegmentum of the midbrain into the large extrapyramidal systems including rubrobulbar, rubrospinal, tegmentobulbar and tegmentospinal tracts. The fact that rubrospinal and tegmentospinal paths are predominantly crossed is consistent with the experimental results of contralateral body movements obtained upon stimulation of the cingulate gyrus. Hess, Bürgi and Bucher ('46), Crosby ('56), and Crosby and Carey ('58) have found that stimulation in the lateral tegmental area of the midbrain gives rise to head and neck, face and eye movements. This is one of the tegmental regions of the midbrain (fig. 9, E, F) in which the corticotegmental paths from the

cingulate gyrus were found to terminate conspicuously. It is interesting to note that the large proportion of the results of stimulation obtained from the additional motor areas shows a dominance of homolateral face and contralateral body movements. This agrees with the current work upon the cingulate gyrus.

Extraocular movements were essentially coordinated with those of the entire head and neck. It was found in the microscopic study that rich association connections existed between primary and secondary motor eye fields and the cingulate gyrus. The regions above and below the principal fissure and area 19 received fibers from the cingulate gyrus. It was also apparent that some of the corticotegmental paths were entering the oculomotor nucleus (protocols 6, 7, 8, 9, 12) and the interstitial nucleus of the medial longitudinal fasciculus. Closure of the eyelids was bilateral, rather than homolateral. It was present particularly when the head and the neck were directed downward and forward, or upward and backward. This pattern of facial response might be postulated as indicating that corticobulbar and tegmentobulbar tracts subserving the cingulate gyrus are crossed and uncrossed to the ventromedial portion of the facial nucleus, and dominantly uncrossed to the dorsolateral part of the facial nucleus. Such an extrapyramidal pathway was suggested by Monrad-Krohn ('24).

In considering the experimental results it is apparent that bilaterality of movement in the total body reaction was also possible. The corticotegmental, tegmentospinal and tegmentobulbar tracts carry crossed components. It will be recalled that the rubrobulbar and rubrospinal tracts are crossed pathways as they begin their caudal course. Finally, a rich intercingulate association tract was present as a component of the cingulum and the corpus callosum. In the account of the experimentation it was noted that bilaterality of movement was elicited more often from the dorsal surface of the cingulate gyrus, and homolateral or contralateral movements were more related to the ventral surface of the gyrus. As a stimulus was applied to the dorsal surface of the gyrus, it approximated

the portion of the cingulum which carried the short, associa-
tion fibers to adjacent primary and secondary motor areas,
as well as those between the cingulate gyri. The ventral sur-
face of the cingulate gyrus was that which overlay the portion
of the cingulum carrying long anteroposterior, posteroante-
rior and subcortical tracts.

There were some connections from the cingulate gyrus to
the caudate nucleus and the globus pallidus. This arrangement
allows the possibility of a relay of somatomotor impulses from
the cingulate gyrus to the basal ganglia and thence by way of
the ventral peduncle of the lateral forebrain bundle into teg-
mental areas of the midbrain. The pathway of impulses from
this last point has been discussed in the first paragraph of
this section. The few connections found from the cingulate
gyrus to the anterior nuclear group of the dorsal thalamus do
not appear to be great enough to suggest that the somatomotor
results are a part of interthalamic connections and relays
which discharge into the extrapyramidal system by way of the
basal ganglia (Showers, '58) to be functional in diencephalic
epilepsy.

However, both acute and chronic experimental evidence in-
dicates that the cingulate gyrus may serve as an epileptogenic
focus. A multiplicity of intercortical connections exists with
primary and secondary motor areas already known in the
study of epilepsy. Epilepsy is associated with clinical syn-
dromes involving the cingulate gyrus (Ironside and Gutt-
macher, '29; LeBeau, '54). Dunsmore and Lennox ('50) found
that they could produce ipsilateral or bilateral seizures in cats
and monkeys by stimulation of the cingulate gyrus. Andy and
McChinn ('57) obtained cingulate gyrus seizures that were
propagated to the opposite hemisphere in their electrographic
study of the stimulation of implanted electrodes in unanesthe-
tized cats. French, Germandt and Livingston ('56) included
the complete gyrus in epileptogenic cortical zones after ex-
perimentation on macaque monkeys.

The movements produced by the stimulation of the cingulate
gyrus occurred independently of adjacent primary and second-

ary motor areas. However, the anatomical connections indicated that short association pathways, both afferent and efferent to the cingulate gyrus existed, which related the superior frontal and parietal convolutions and the orbital gyri with the cingulate gyrus. Other intercortical paths which the protocols document, form a similar relationship for the cingulate gyrus with the middle and inferior frontal convolutions, the inferior parietal convolution, the superior, middle, inferior temporal, and hippocampal gyri, and the hippocampus, and probably with the insula. These include the additional motor areas previously mentioned. There is a basis for concluding that when multiple additional motor areas are destroyed, the motor defect becomes greater. Homolateral facial weakness did not appear until several contralateral second motor areas were added to the cingulate lesion. This was also true of the incidence of upper and lower extremity apraxia. Weakness of the extremities did appear ipsilateral to the cingulate lesion and contralateral to other additional motor area lesions.

It is recognized that many of the somatic movements were included in the expression of emotional reaction. As these occurred during the acute phase of the experimentation, they were emotional reactions without emotion as it is interpreted to be a blend of cortical associations. Fulton ('49) defines the region rostral to the precentral motor cortex as the discrete functional division of the cerebrum concerned with autonomic integrations, emotions, and certain higher intellectual functions. The intercortical pathways to the cingulate gyrus appear to permit it to function in elaboration of an emotion and in an emotional expression. Barris and Schuman ('53) and Kennard ('55) point out that apathy proceeding to stupor, and to coma, akinesia, and mutism (Marchifara syndrome) may result when portions of the anterior cingulate gyrus are damaged by tumor in the human. The animals most quiet following cingulate destruction were those in which the lesion involved the supracallosal portion of area 24. In the majority of the animals, there was an increased, rather than decreased, overt expression of emotion involving numerous somatic

movements. The intensity of the reaction was greater in the presence of the examiner. This suggests that there might have been less cortical inhibition of emotional expression following the more rostrally and more caudally placed cingulate lesions. It might be mentioned here that some of the best results in psychosurgery have been obtained in cingulectomy when obsessive-compulsive neuroses have been a part of the reaction pattern of the patient (LeBeau, '54). In the 50 cases reported, the improvements followed cases presenting a pattern of chronic epilepsy, irritability, aggressiveness, violence and agitation. It may be analogized that the hyperkinesia and other overt expression in the experimental animals in this study resembled the patients reported by Le Beau. It is possible that an imbalance in the inhibitory function of the cingulate gyrus as related with the frontal cortex would produce the extremes observed in the clinical and experimental work, and that the syndrome observed was partly dependent upon the location of the disability in the cingulate gyrus. Finally, that as the disability was increased by surgical intervention, it was possible to restore a state of balance to the function of the frontal cortex.

Visceral phenomena

Continuing with the concept that has been suggested in the previous section on somatic phenomena, visceral changes will be presented as a part of the complex adjustment of the animal to its surroundings under the general connotation of emotional reaction. Herrick ('56) distinguishes 6 levels of visceral function in the adaptation of a living organism to its environment. In the first, there is a measure of intrinsic tonicity and automaticity characteristic of all living substances, particularly human muscle and viscera. Secondly, visceral functions are highly susceptible to clinical controls of the hormones by way of body fluids. Thirdly, a local regulation of the viscera is facilitated by intrinsic ganglionated plexuses. Fourth, a central regulation of the plexuses is accomplished through cranial and spinal nerves. Fifth, the cerebral visceral centers

such as the hypothalamus are superimposed. Sixth, all those lower levels are under some control by the cerebrum. Papez ('37) elaborated upon this last factor as he proposed a mechanism for emotion which postulated the cortical origin of emotion as being built up in the hippocampus and transferred to the mammillary body. From this structure impulses entered the mammillothalamic tract to reach the anterior nuclear group of the dorsal thalamus. Anterior thalamic radiations carried the impulses thence to the cingulate gyrus. He looked upon the cingulate gyrus as the receptive region for experiencing impulses coming from the hypothalamus.

Temperature changes were a prominent part of the animal's visceral responses. ''Hot with rage'' and ''cold with anger'' are not unusual expressions. With the latter appropriately would come the trembling, or the shivering, and the vasoconstriction to elevate the body temperature. With the former appropriately would come the sweating and vasodilation to lower body temperature. It is likewise a common descriptive phrase to say ''one breaks out in a cold sweat.'' The visceral variables may connotate that parts of the emotional reaction can be set off without logical autonomic interactions. ''One's hair may stand on end'' and ''goose flesh'' occurs in a number of persons with extremes in emotional reactions. Cardiovascular changes, shivering, and piloerection are documented in the work of Smith ('41), ('45), Ward ('48) and Kaada ('51). Similar alterations are noted in the stimulation of the anterior cingulate gyrus in man by Pool and Ransahoff ('49) and Pool ('54). The hypothalamic areas concerned in the regulation against heat and cold (Ranson, '40) are involved in the termination of the corticohypothalamic connections from the cingulate gyrus (Protocols 6, 7, 8, 9, 11, 12). The pathway which regulates against heat arises in the preoptic and anterior hypothalamic area, as the anterior hypothalmotegmental tract it passes to subrubral gray, then reticular or tegmental fasciculi carry the impulses to the lateral ventral tegmental nucleus of the pons. From this last nucleus there arise ventral and lateral reticulospinal tracts which are

responsible for sudomotor and vasodilator activity on face and body. The ventromedial hypothalamic nucleus and posterior hypothalamic area regulate against cold through the posterior hypothalamotegmental tracts to subrubral gray. The connections from this region cause piloerection and vasoconstriction. These pathways are described in detail by Crosby and Woodburne ('51).

Respiratory changes occurred with the emotional expression in the experimental animals. These included increases in rate, decreases in rate, noisy respiration, vocalization, and apnea. An angry, or fearful, person may breathe rapidly, or slowly. Some individuals will hold their breath under emotional stress. There are people who are voluble with their anger, or fear, and those who are unable to speak. Hypothalamic pathways to brain stem respiratory centers are influenced by connections from the cingulate gyrus. Increased rate (Furstenberg and Crosby, '48) can be produced by the anterior and dorsal hypothalamic areas (protocols 6, 7, 8, 9, 11, 12) transmitting nerve impulses over the dorsal longitudinal fasciculus and hypothalamotegmental tracts to the pontine and medullary respiratory centers. Pathways from the posterior hypothalamic area and periventricular gray to the brain stem respiratory centers tend to inhibit respiration (Furstenberg and Crosby, '48). These authors take pains to emphasize the complexity of the respiratory mechanism, and that the neuronal arcs which govern it are susceptible to emotional stimulation. Turner ('54) obtained apnea by stimulation of the ansa lenticularis and zona incerta, among other structures. It will be recalled that corticohypothalamic tracts (fig. 9, B, C) are travelling with the ansa lenticularis fibers, and turn downward to the hypothalamus in the field of Forel at the medial side of the zona incerta. The intercortical association pathways between the orbital gyri (areas 12 and 13) and the cingulate gyrus (fig. 6, A) were evident in this microscopic study. The orbital gyri have previously been found to control respiration (Kaada, '51; Turner, '54 and Anand and Dua, '56). Pool and Ransahoff ('49) and Pool ('54) demonstrated that stimulation

of the anterior cingulate region in the human decreased respiration. Kaada ('51) includes anterior limbic and subcallosal areas in those fields of cortex the stimulation of which inhibits respiration, and the posterior part of the anterior limbic area in the acceleration of respiration. Other workers who have obtained similar results relevant to respiration include Smith ('41), ('45), Ward ('48), Dunsmore and Lennox ('50) and Sloan and Kaada ('53). Excepting Dunsmore and Lennox these investigators commented upon vocalization in terms of dependency upon respiratory alterations.

Increases in salivary and mucous secretion are possible by the cingulate connections into the hypothalamus. The hypothalamic centers give rise to the dorsal longitudinal fasciculus. This fasciculus then passes toward cranial nerve nuclei (Crosby and Woodburne, '51).

Pupillary dilatation has been demonstrated experimentally from stimulation of the cingulate gyrus in cat by Siebens and Woolsey ('46) and in monkey by Smith ('41), ('45), Ward ('48), Kaada ('51). According to Siebens and Woolsey ('46) and Ward ('48) this effect occurs after section of the oculomotor nerve. Such active dilatation would be possible through the corticohypothalamic paths from the cingulate gyrus terminating in the hypothalamic areas (Hodes and Magoun, '42), giving rise to the posterior hypothalamotegmental tracts which pass to the tegmental centers that form the medial reticulospinal tracts regulating the thoracolumbar autonomic outflow. Widely dilated pupils can be observed in the very angry and very fearful person.

The waking state (Magoun, 52) is frequently interpreted as dependent upon the arousing influences of afferent sensory information upon cerebral cortex. It might be suggested that the alternate sleep and hyperkinesia seen in the experimental animals in this study were not incompatible, rather additive, to this concept. The greatest influence culminating in sleep occurred when sizeable lesions were present in the supracallosal portion of the cingulate gyrus. Andy and McChinn ('57) found EEG sleep spindles-appeared readily from the supra-

callosal part of the cingulate gyrus in unanesthetized cats. This was also the region from which the greatest variety of somatic movements were obtained. It might be possible that a driving influence of the secondary cortical centers discharging normally into the extrapyramidal system and hypothalamus is removed. Thus, part of the cortical efferent mechanism of the waking state is interrupted and sleepiness results. Relative to the cingulate gyrus this would also remove the mechanism for a reverberating circuit that exists from the mammillary bodies of the hypothalamus into mammillothalamic tract to the anterior nuclear group of the dorsal thalamus through the anterior thalamic radiations to the cingulate gyrus. Jasper ('49) considers this to be an important secondary afferent relay system in the diffuse projection systems which cause some of the excitation of the cerebral cortex. Hunter and Jasper ('49) found that they could produce running and climbing activity of fear, flight and rage in unanesthetized cats by stimulation of electrodes implanted in the mammillothalamic tract.

It was obvious that the experimental animals readily compensated for such a sleep reaction, since it was transient. The parallel might also be drawn that somatic disability from loss of additional motor areas is equally transient. The hyperkinesia appeared as a part of the behavior of the animals observed, whether it was quiet or noisy. Here there seems to be a release from the possibly inhibitory influence of the cingulate gyrus upon the driving effect of the cortical association areas discharging to the hypothalamus for its subsequent mediation as an emotional reaction. The sites of lesions producing the most intense hyperkinesia were in the rostral and caudal portions of the cingulate gyrus. Those areas were related to one another by intracingulate tracts (p. 270). Both areas gave rise to autonomic phenomena upon appropriate stimulation. And it has been observed that they were connected to the hypothalamus. The cingulate gyrus was also well related to surrounding cortical areas considered responsible for initiating emotional reactions, particularly to those areas of the frontal

cortex receiving from the medial thalamic nucleus (Pribram, Chow and Semmes, '53, Showers, '58). In many respects, hyperactivity in the experimental animals resembled sham rage in that it was inappropriately excessive in terms of the environmental stimuli. This circumstance might also be compared to the intentional dulling of emotional expression which is the effect desired in the psychosurgery involving the severing of the anterior thalamic radiations (Freeman and Williams, '51).

SUMMARY

1. Analysis of 20 experiments on 15 macaque monkeys is presented. This demonstrated that stimulation of the cingulate gyrus produced a pattern of both somatic and visceral behavior. The most rostral and most caudal portions of the gyrus gave rise to cardiovascular, respiratory, thermal and secretory changes, and pupillary dilatation. All parts of the gyrus, when stimulated, resulted in changes in facial expression. Excitation of the supracallosal area 24 of the gyrus from a rostral to caudal direction caused movements in the upper extremities, chest, abdomen, lower extremities and tail. Excitation of the supracallosal area 23 of the gyrus from a rostral to caudal direction resulted in the same body movements in a reversed order. Thus, the cingulate gyrus qualifies as an additional motor area and cortical autonomic regulator.

2. Anatomical connections of the cingulate gyrus were described in this study.

(a) Intracingulate paths related the rostral parts of the gyrus, including subcallosal gyrus, area 25 and supracallosal area 24 to the caudal parts of the gyrus, including supracallosal areas 23, 29, and isthmus, and conversely. These same subdivisions were associated by commissural fibers in the corpus callosum with the comparable parts of the opposite cingulate gyrus.

(b) Other intercortical paths connected the cingulate gyrus with the temporal lobe, excluding the amygdaloid nuclei, with the frontal lobe, the parietal lobe and the preoccipital area.

(c) Some corticostriatal projections were found from the cingulate gyrus to the caudate nucleus and globus pallidus.

(d) A few corticothalamic paths from the cingulate gyrus lead to the anterior nuclear group of the dorsal thalamus, essentially into the nucleus anteroventralis.

(e) Corticohypothalamic connections could be traced from the cingulate gyrus which travelled with the fibers of the diencephalic periventricular system, the inferior thalamic peduncle and the ventral peduncle of the lateral forebrain bundle.

(f) A prominent corticotegmental group of fibers was found in the fascicles of the ansa and fasciculus lenticularis.

(g) A large corticonigral connection from the cingulate gyrus to the medial portion of the substantia nigra is described.

3. The cingulate gyrus is discussed in terms of its convulsive seizure potential.

4. An attempt is made to explain the acute and chronic results of the experimentation as components of emotional expression. It was suggested that the extremes of somatic and visceral phenomena came about as an imbalance was created in the association of the cingulate cortex with surrounding cortical regions, particularly with the frontal lobe. Finally, part of the relationship of the cingulate gyrus to the frontal cortex may be of an inhibitory nature.

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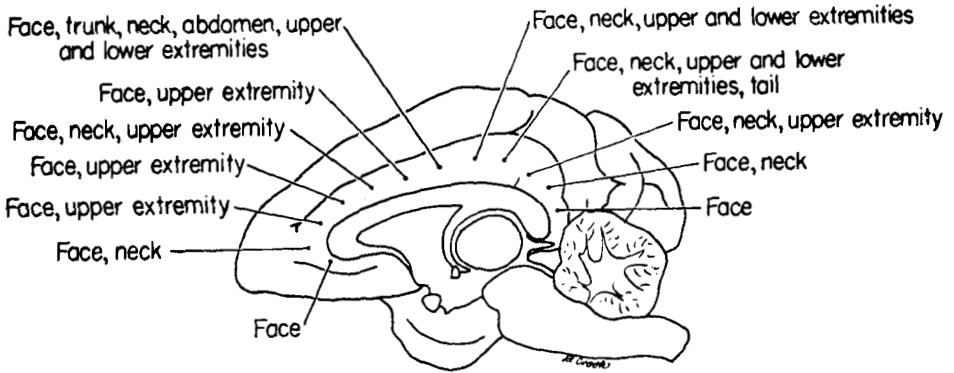
AG, anterior nuclear group of dorsal thalamus

C, cingulum

CC, corpus callosum

CG, cingulate gyrus

CN, caudate nucleus

CP, cerebral peduncle

CR, corona radiata

DP, diencephalic periventricular system

F, fornix

FR, fasciculus retroflexus

GP, globus pallidus

GR, gyrus rectus

H, hypothalamus

HG, hippocampal gyrus

HI, hippocampus

IC, internal capsule

ITP, inferior thalamic peduncle

III, oculomotor nerve roots

LFB, lateral forebrain bundle (fasciculus lenticularis and ansa lenticularis)

MT, mammillothalamic tract

MTG, middle temporal gyrus

NVA, nucleus ventralis anterior of dorsal thalamus

NVL, nucleus ventralis lateralis of dorsal thalamus

NVP, nucleus ventralis posterior of dorsal thalamus

O, operculum

OG, orbital gyrus

OL, occipital lobe

OT, optic tract

P, pulvinar

PF, principal fissure

RN, red nucleus

SC, sulcus cinguli

SFC, superior frontal convolution

SPC, superior parietal convolution

SG, subcallosal gyrus

SM, stria medullaris

SN, substantia nigra

STG, superior temporal gyrus

STN, subthalamic nucleus

T, tapetum

VT, ventral tegmental area

ZI, zona incerta

PLATE 1

EXPLANATION OF FIGURE

4   A, Diagram summarizes the somatomotor responses from stimulation of the cingulate gyrus. B, Animal C-S-3 before stimulation of the right cingulate gyrus. Note the right side of the face and the left arm. Enlargement made from 16-mm movie film. C, Animal C-S-3 after stimulation of the right cingulate gyrus. D, Animal C-S-6 during stimulation of the left cingulate gyrus demonstrates pupillary dilatation on the right side, bilateral movement of the facial musculature, and the head elevated and turned toward the stimulation. Enlargement made from 16-mm movie film. E, Animal C-S-1 shows the aggressive attitude and piloerection after ablation of the cingulate gyrus. Enlargement made from 16-mm movie film. All parts of this figure are borrowed from Showers and Crosby ('58).

Face, trunk, neck, abdomen, upper and lower extremities

Face, neck, upper and lower extremities

Face, upper extremity

Face, neck, upper and lower extremities, tail

Face, neck, upper extremity

Face, neck, upper extremity

Face, upper extremity

Face, neck, upper extremity

Face, neck

Face, upper extremity

Face

Face, neck

Face

A

B

C

D

E

5   A, Photomicrograph of the brain of C-S-8 shows the degeneration extending
    from the superior frontal convolution (area 8) to the cingulate gyrus. Marchi
    preparation. $\times$ 13.8. B, Photomicrograph of the brain of C-S-11 shows the
    degeneration from the cingulate gyrus to the superior parietal convolution
    (area 5). Marchi preparation. $\times$ 14.4.
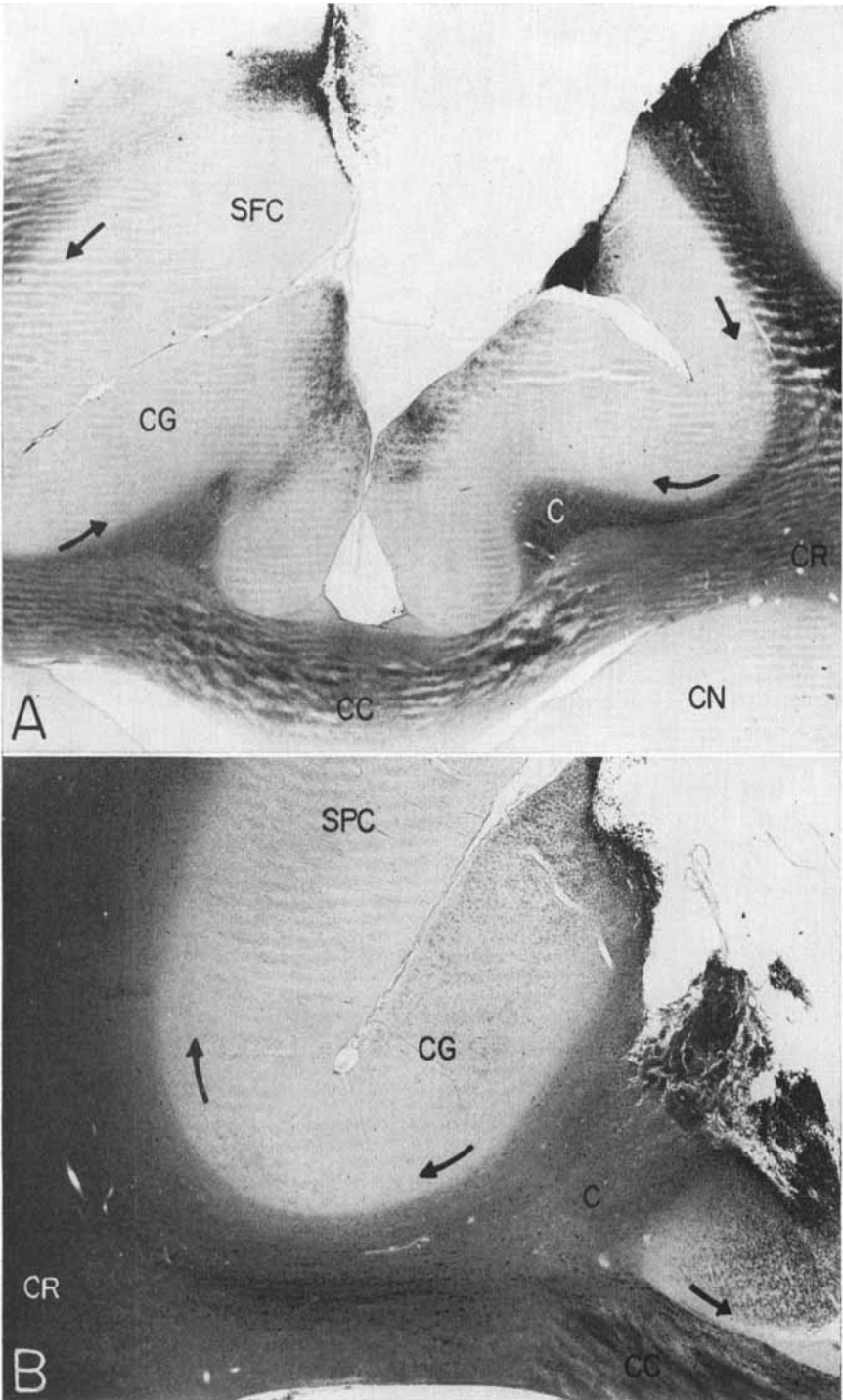
6 A, Photomicrograph of the brain of C-S-9. Degenerating fibers can be seen extending from the cingulate gyrus into gyrus rectus (area 14), orbital gyri (areas 12 and 13) and frontal operculum (area 45). Marchi preparation. × 8.2. B, Photomicrograph of the brain of C-S-12. Corticonigral pathways from the cingulate gyrus can be viewed coming through the posterior limb of the internal capsule to the medial portion of the substantia nigra. Marchi preparation. × 8.2.
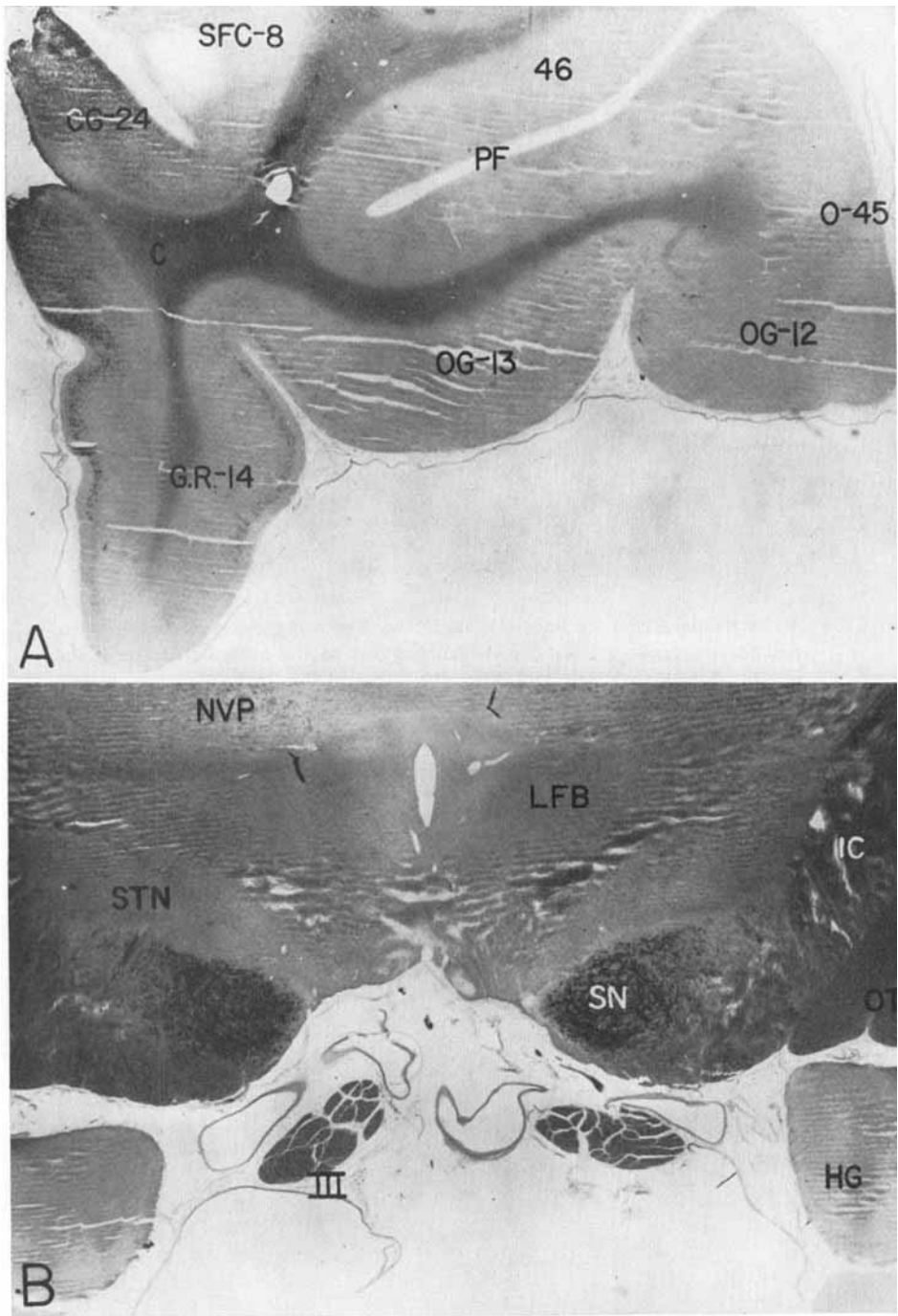
7   A, Photomicrograph of the brain of C-S-8. The arrows show the pathway of
the fibers extending from the cingulate gyrus to the anterior nuclear group
of the dorsal thalamus and into the diencephalic periventricular system.
Marchi preparation. $\times$ 8.2.   B, Photomicrograph 250 μ caudal to A.   C,
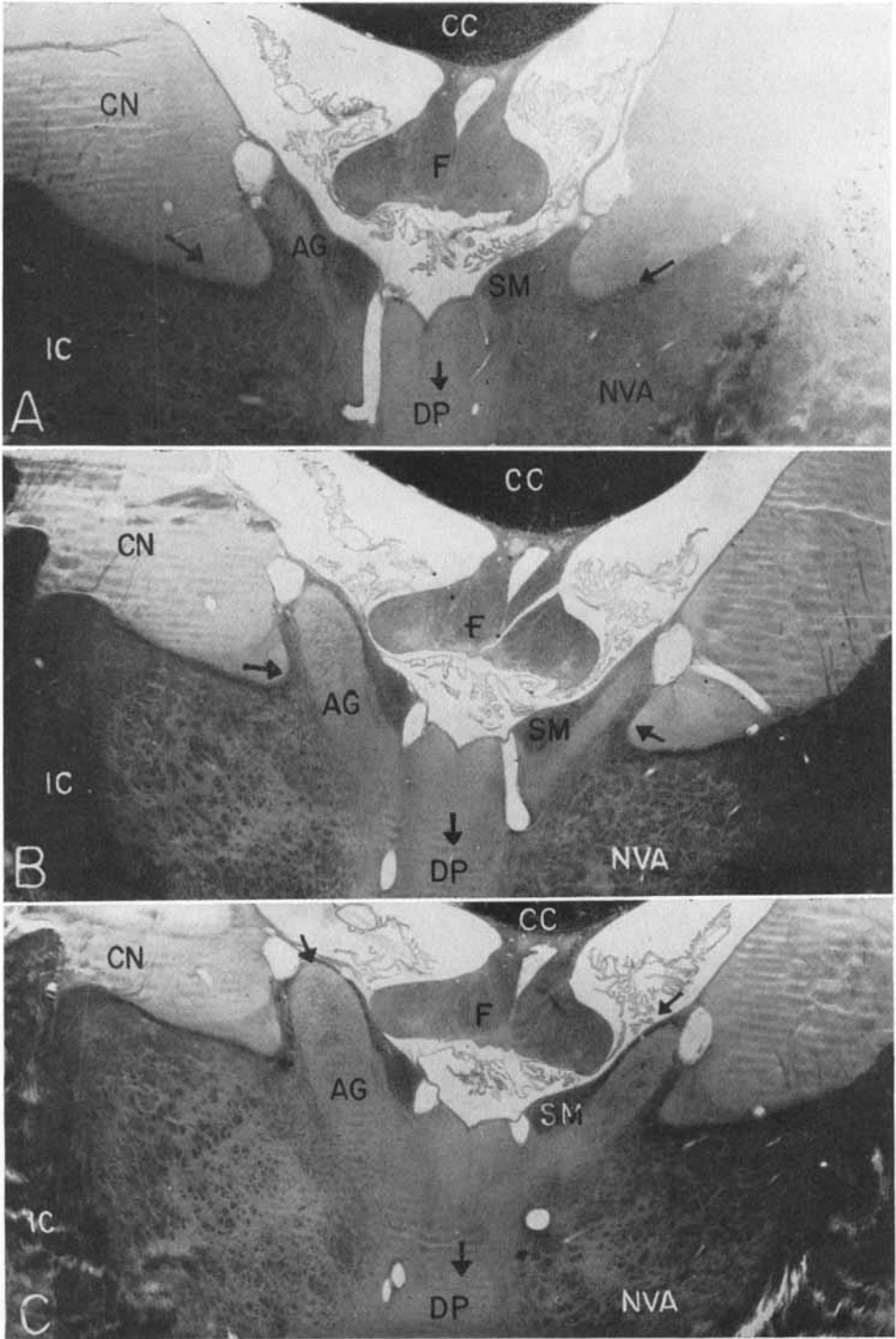Photomicrograph 250 μ caudal to B.

8 A, Photomicrograph of the brain of C-S-7 shows a lesion (L) in the medial division of the globus pallidus. Degeneration extends into the fibers of the lenticular fasciculus as it becomes the ventral peduncle of the lateral forebrain bundle. Marchi preparation. × 13.8. B, Photomicrograph of the brain of C-S-11. Degenerating fascicles in the cingulum are travelling medial to the tapetum toward the alveus in the temporal lobe. Marchi preparation. × 8.2. C, Photomicrograph of C-S-6 shows corticotegmental fibers in the position of the ventral peduncle of the lateral forebrain bundle. Compare the size and medulation of the fibers with those illustrated in A. Marchi preparation. × 8.2.
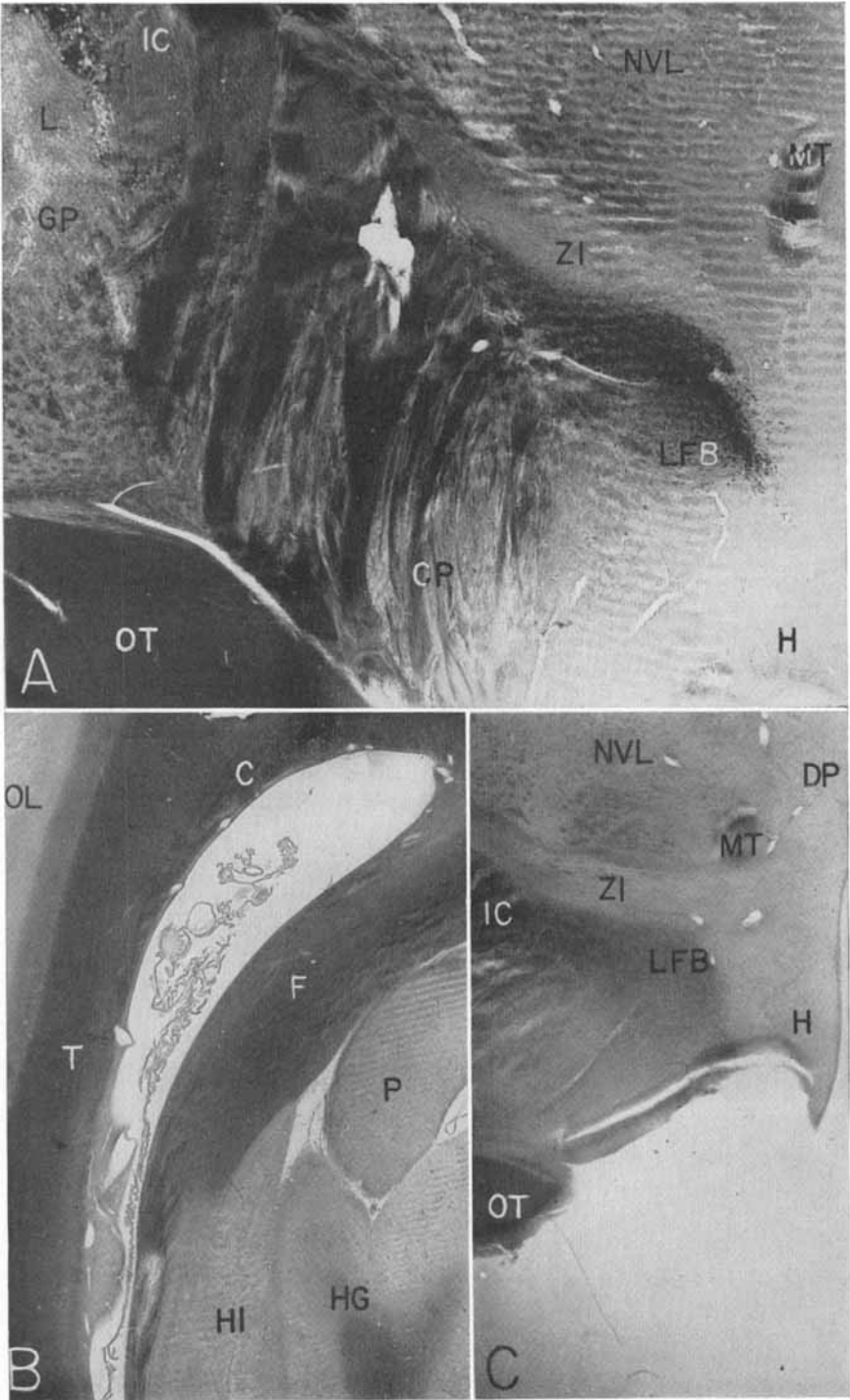
9   A, Photomicrograph of the brain of C-S-6 showing corticotegmental fibers collecting in the medial segment of the globus pallidus. Marchi preparation. × 8.2. B, Photomicrograph 250 μ caudal to A. C, Photomicrograph 500 μ caudal to B. D, Photomicrograph 500 μ caudal to C. E, Photomicrograph 4000 μ caudal to D. Small letter d indicates the collection of degenerating fascicles in the lateral tegmental area of the midbrain. F, Photomicrograph 2750 μ caudal to E. Small letters d indicate the collections of degenerated fascicles in the lateral and ventral tegmental areas of midbrain.
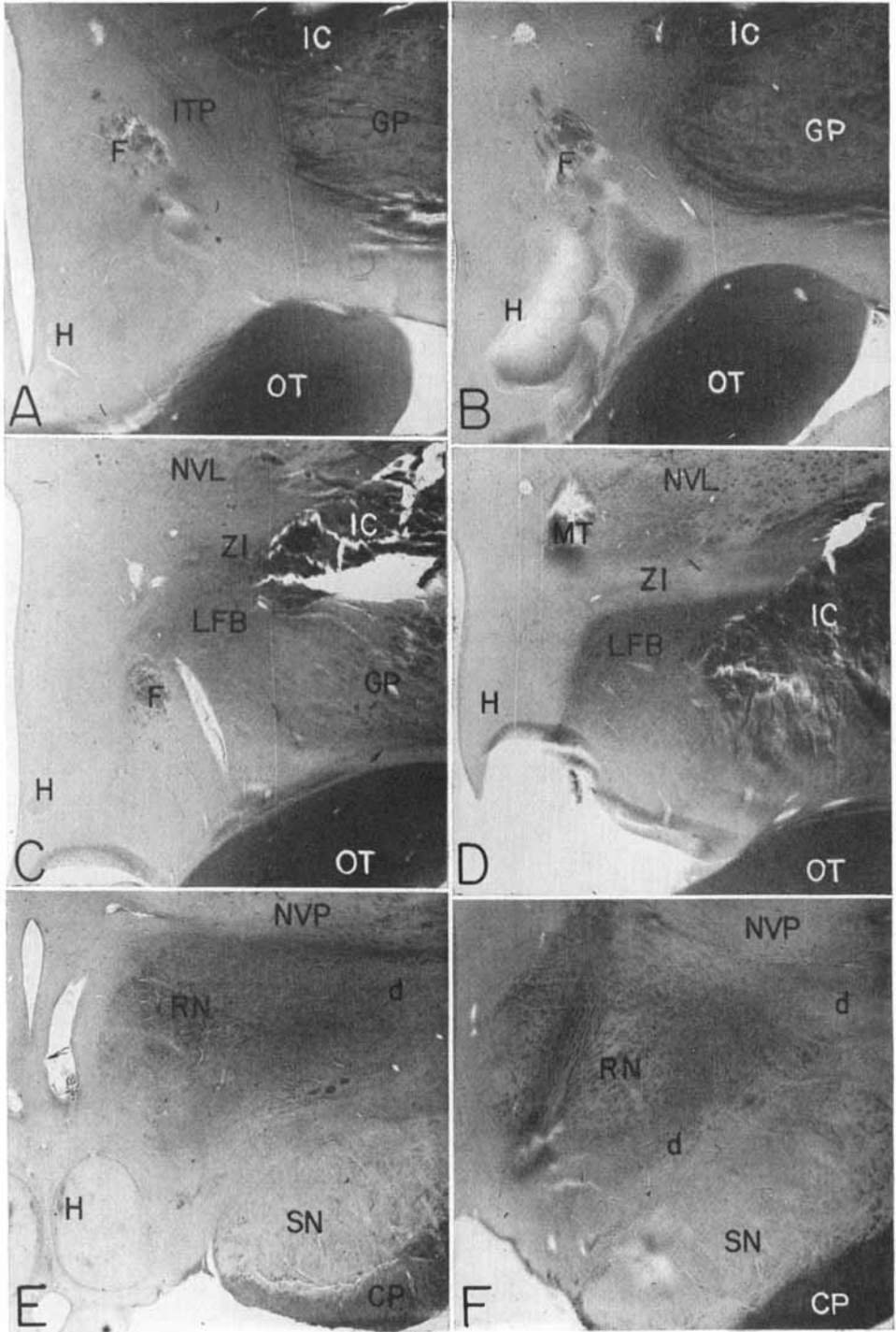
10 A, Photomicrograph of the brain of C-S-6 showing corticotegmental fibers in
the ventral peduncle of the lateral forebrain bundle turning downward toward
the hypothalamus. The square outlines the area enlarged in B. Marchi
preparation. $\times$ 8.2. B, Photomicrograph of the square outlined in A. $\times$ 410.
C, Photomicrograph of the brain of C-S-6 showing corticotegmental fibers
terminating in the ventral tegmental region of the midbrain. This photograph
is the right one-half of the picture in figure 9, F. The square outlines the
region enlarged in figure 10, D. Marchi preparation. $\times$ 8.2. D, Photomicro-
graph of the region outlined in C. $\times$ 410.