Microsurgical and Fiber Tract Anatomy of the Nucleus Accumbens

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BACKGROUND: The nucleus accumbens (NAc) has been a target for deep brain stimulation (DBS) in the treatment of depression and obsessive-compulsive disorder (OCD).

OBJECTIVE: To examine the anatomy and connections of the NAc using a fiber dissection technique.

METHODS: Ten human brains and 2 whole cadaveric heads were examined by fiber dissection technique and ×6 to ×40 surgical magnification. The NAc was examined from the lateral, medial, superior, and inferior sides to define its fiber connections and relationships with adjacent cortical and subcortical structures. Magnetic resonance imaging (MRI) with 1-mm slices was used to define its neuronavigation coordinates.

RESULTS: Eight tracts, the uncinate fasciculus, cingulum, stria medullaris thalami, fornix, diagonal band of Broca, stria terminalis, medial olfactory stria, and forceps minor, form a capsule around the anterior, inferior, and medial sides of the NAc. The uncinate fasciculus connects along the inferior and adjacent part of the medial side of the NAc, the cingulum and diagonal band along the medial surface, the medial olfactory stria along the posteromedial and adjacent part of the inferior surface, the forceps minor along the anteromedial surface, and the stria terminalis, fornix, and stria medullaris along the posterosuperior surface. The subcortical gray matter related to the NAc includes the septal nuclei, indusium griseum, substantia innominata, caudate nucleus, and hypothalamus. The cortical areas communicating with and overlying the NAc are reviewed.

CONCLUSION: An increased understanding of the fiber connections and neural relationships of the NAc should allow more accurate DBS targeting for the treatment of psychiatric disorders.

KEY WORDS: Anterior commissure, Basal forebrain, Deep brain stimulation, Fiber dissections, Functional neurosurgery, Limbic system, Nucleus accumbens

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The nucleus accumbens (NAc), a gateway to the basal ganglia's limbic-motor interface, is involved in cognitive, emotional, and psychomotor functions and has been shown to be a hub in some psychiatric disorders including depression, obsessive-compulsive disorder (OCD), severe anxiety, and addictive behaviors.[1-3] The NAc is part of the ventral striatum, which, based on the classification by Heimer and Wilson[4] in 1975, also includes the olfactory tubercle and the adjacent part of the head of the caudate nucleus. The detailed mechanisms underlying major depression, OCD, and addiction are not completely understood, but they are thought to represent a failure of ventral striatum inhibition and dysfunction of the limbic loop of the corticostriatal circuit, of which the NAc is a network.[1,3,5]

ABBREVIATIONS: BA, Brodmann area; **DBS,** deep brain stimulation; **NAc,** nucleus accumbens; **OCD,** obsessive-compulsive disorder; **SLF,** superior longitudinal fasciculus

The NAc, based on animal studies, is microscopically divided into a shell located on the ventromedial periphery, related to the limbic system, and a core located dorsolaterally, related to the extrapyramidal system.[6,7] The core is suggested to be involved in guiding behavior toward a specific goal based on learning and the shell in unconditioned reward-seeking behaviors. In primate and human brains, the shell and core seem to function together rather than independently.[8]

The NAc and related structures have been targets for deep brain stimulation (DBS) in the treatment of major depression and OCD.[1,5,8,9] Placement of DBS in the NAc and its related cortical (eg, subgenual anterior cingulate and subcallosal cortices) and subcortical gray matter (eg, amygdala, septal nucleus) and its connection pathways (eg, uncinate fasciculus, cingulum) have resulted in remission rates as high as 55% in drug-resistant major depression and 75% in OCD.[9,10] An understanding of the connections of the NAc is basic to understanding the pathogenesis and treatment of psychiatric disorders. This study examined the NAc, its connections, and related cortical and subcortical gray matter using a fiber dissection technique.

METHODS

Ten formalin-perfused human brains (20 sides) and 2 cadaveric heads were received from our anatomic board and preserved in a 70% alcohol solution between and during dissections. The arachnoid and surface vessels were removed from the brains. All specimens were refrigerated at −16°C for 2 weeks.[11,12] After thawing the brains, the fiber dissections were performed with microdissectors under ×6 to ×40 magnifications provided by a surgical microscope.[13,14] Before starting the cranial dissections, 3-T magnetic resonance imaging (MRI) with 1-mm slices was obtained for a magnetic resonance neuronavigation system. After exposing the NAc, the size, shape, and position of the NAc and related cortical and subcortical gray matter and the white matter fiber connections of the NAc were examined. Measurements were taken with electronic scales. References to functional studies have been cited at the point that they contribute to the understanding of the function of anatomic structures.

Dissections were completed from 4 directions starting at the lateral, medial, inferior, and superior surfaces of the brain. For lateral to medial dissections, the cortex and subcortical U-fibers were removed to expose the superior longitudinal fasciculus (SLF) II and III, the inferior frontal gyrus was removed to expose the insular cortex, and, one by one, the insular cortex, extreme capsule, claustrum, external capsule, and putamen were removed to expose the globus pallidus, internal capsule, anterior commissure, and NAc. Medially to laterally, the anterior cingulate and subcallosal cortices, paraterminal gyrus, and subcortical U-fibers were removed to expose the cingulum and NAc. Superiorly to inferiorly, the cortex, subcortical U-fibers, SLF II, corona radiata, and the head of the caudate nucleus were removed to expose the anterior commissure and the NAc. Inferiorly to superiorly, the olfactory tubercle, gyrus rectus, medial orbital gyrus, subcortical U-fibers, and the ventromedial part of the uncinate fasciculus were removed to expose the NAc and substantia innominata.

RESULTS

Location

The NAc is located in the medial part of the basal forebrain below the head of the caudate nucleus (Figure 1). Its superolateral edge at its junction with the laterally placed substantia innominata has been considered to be at the inferior edge of the anterior limb of the internal capsule.[15-17] In this study, we found the anterior commissure to be a reliable landmark defining the posterosuperior and superolateral margins of the NAc (Figures 2 and 3). The anterior commissure has 3 parts: a body and anterior and posterior crura. The body of the anterior commissure crosses the midline between the paired crural bifurcations. The anterior crus extends forward to the medial orbitofrontal area, and the posterior crus, which is thicker than the anterior crus, has an occipital extension that blends into the sagittal stratum and a temporal extension that runs to the temporal pole. The anterior crus of the anterior commissure projects forward at a right angle to the posterior crus along the superolateral margin of the NAc. The anterior crus courses forward just below the inferior edge of the anterior limb of the internal capsule (described by Klingler[11,12] as the fasciculus marginalis frontalis), which has been used to approximate the position of the lateral edge of the NAc and the border between the NAc and substantia innominata (Figure 2B). Removing the anterior limb of the internal capsule exposes the head of the caudate at the superior border of the NAc (Figure 2C). In summary, the NAc is located anterior and inferior to the superior edge of the body of the anterior commissure and inferior and medial to the anterior crus.

The lateral, superior, and posterior surfaces of the NAc blend without clear demarcation into the substantia innominata, caudate nucleus, and hypothalamus, respectively. The medial, anterior, and inferior surfaces have a round shape. The posterior surface of the NAc, located at the coronal level of the anterior edge of the body of the anterior commissure and lamina terminalis, faces the anterior edge of the hypothalamus (Figures 2D and 2E). The lateral surface of the NAc faces the substantia innominata, located below the anteroinferior part of the putamen, and its superior surface blends into the head of the caudate nucleus at the level of the anterior crus of the anterior commissure and lower edge of the anterior limb of the internal capsule (Figures 1-3). The medial, inferior, and anterior surfaces of the NAc are wrapped in a capsule of white matter tracts that can be identified using the fiber dissection technique. The length of the NAc measured in 20 hemispheres, in the anteroposterior plane, averaged 10.89 ± 1.18 mm (range, 8.41-12.52 mm), the width in the mediolateral plane measured 7.38 ± 1.02 mm (range, 5.81-9.76 mm), and the height at the midpoint of the anteroposterior diameter averaged 6.57 ± 0.77 mm (range, 5.51-7.86 mm).

In the lateral view of the cerebrum, the NAc is positioned directly medial to the lower half of the pars triangularis of the inferior frontal gyrus and the lower half of the anterior and middle short insular gyri on the insular surface (Figure 4). In the medial view, the NAc is located lateral to the paraterminal gyrus, the lower half of the subcallosal cortex (Brodmann area [BA] 25), and lateral to the paracingulate cortex (ventral subdivision of BA 32). In the view through the inferior surface, the NAc is located above the posterior part of the gyrus rectus and anterior to the medial olfactory stria and anterior perforated substance. The lateral edge of the NAc is positioned an average of 27.95 ± 2.72 mm (range, 25.41-32.35 mm) deep to the short insular gyri and 3.55 ± 0.30 mm (range,

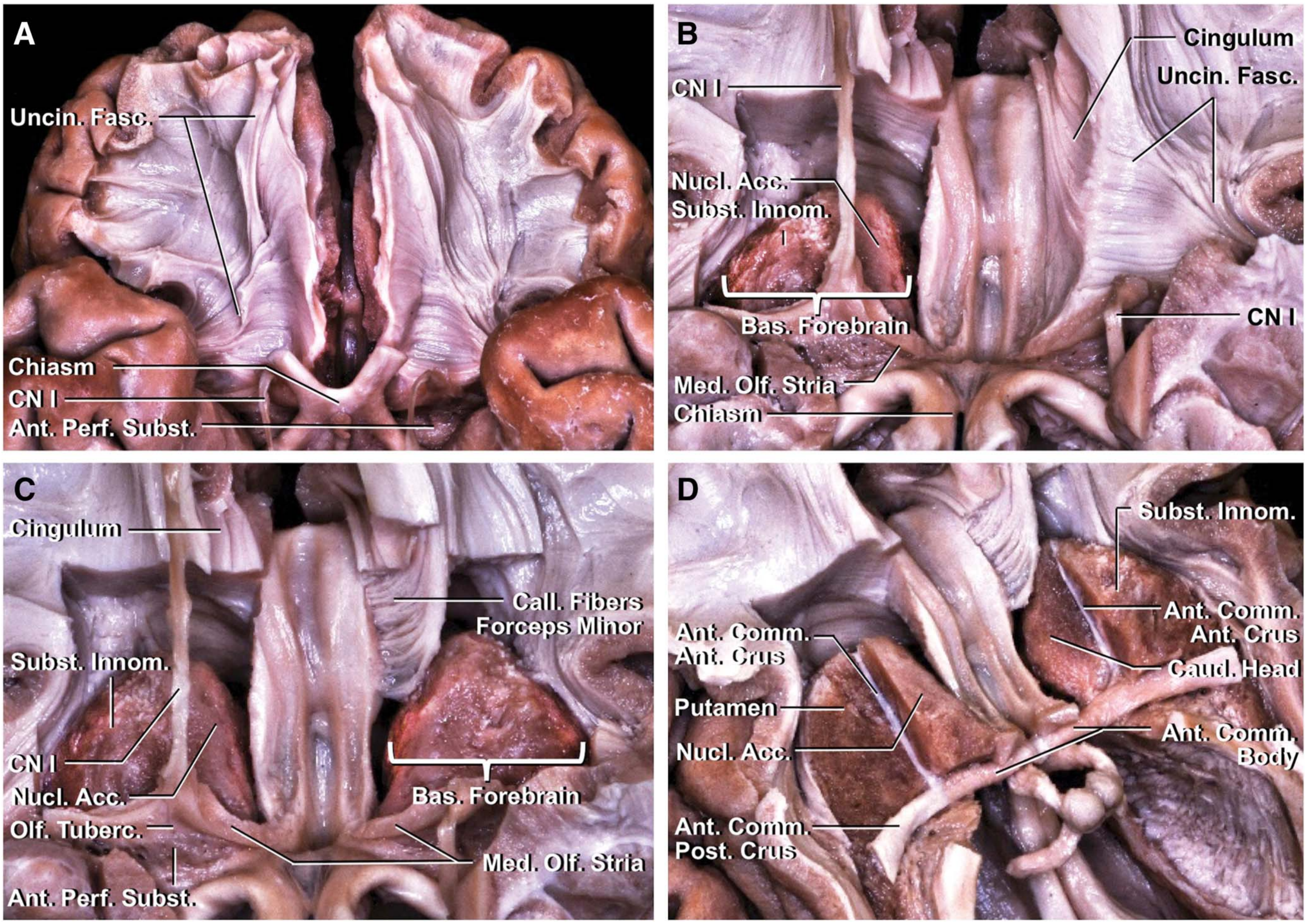
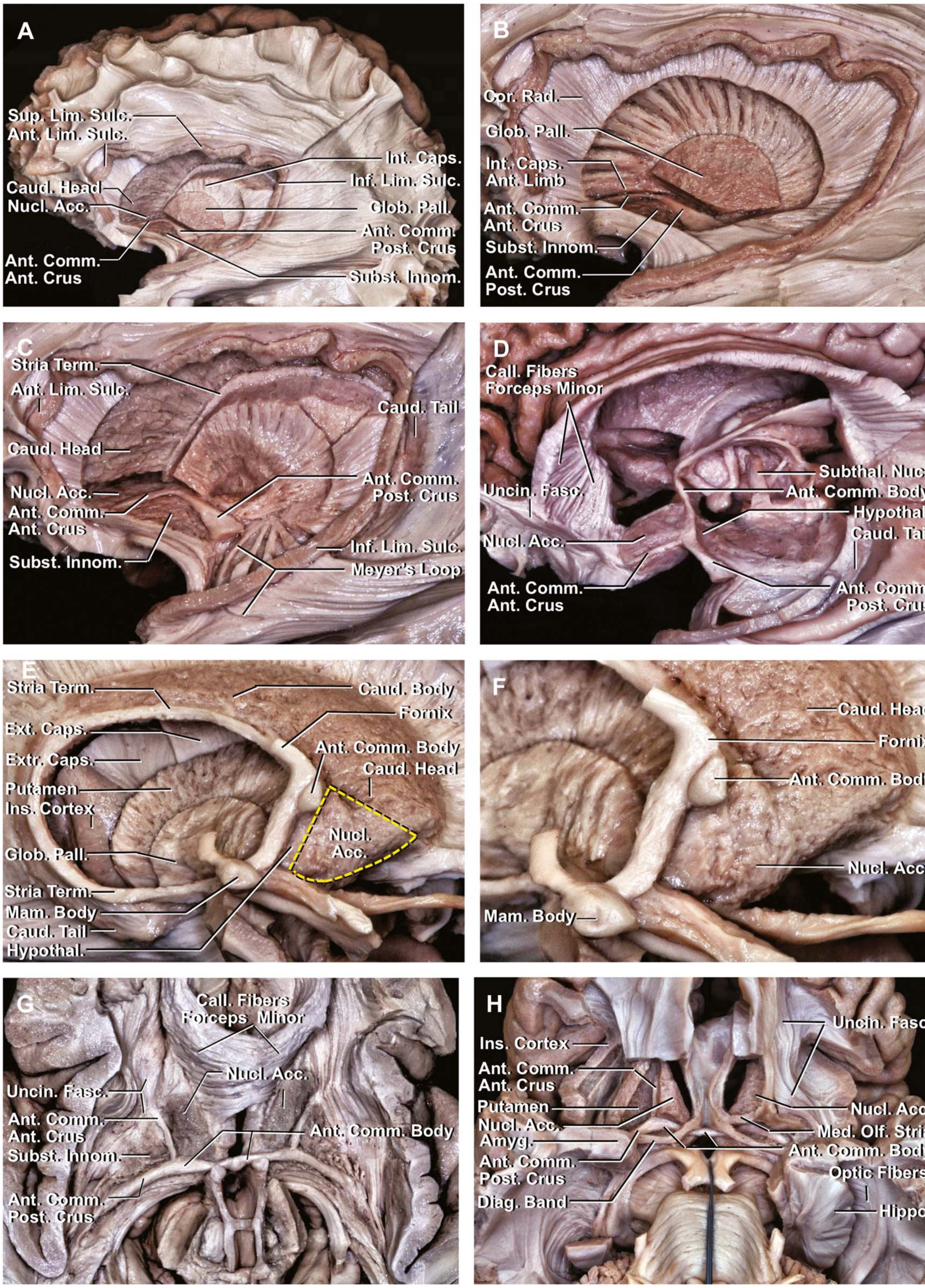


FIGURE 1. *Basal forebrain.* **A**, *inferior view. The basal frontal cortex and U-fibers have been removed to expose the uncinate fasciculus crossing below the basal forebrain. The olfactory nerves have been reflected posteriorly to improve the exposure.* **B**, *the right uncinate fasciculus, cingulum, and callosal fibers have been removed to expose the basal forebrain formed by the NAc medially and the substantia innominata laterally. The optic chiasm and left olfactory nerve have been reflected posteriorly.* **C**, *the left uncinate fasciculus and cingulum fibers have been removed to expose the left NAc, substantia innominata, and forceps minor. The left forceps minor passes along the anteromedial surface of the NAc.* **D**, *right inferior oblique view. The right substantia innominata has been removed to expose the putamen. The left NAc has been removed to expose the caudate head. The upper edge of the border between the NAc and the substantia innominata is along the anterior crus of the anterior commissure, which passes just below the anterior inferior edge of the anterior limb of the internal capsule. Acc., accumbens; Ant., anterior; Bas., basal; Call., callosal; Caud., caudate; CN, cranial nerve; Comm., commissure; Fasc., fasciculus; Innom., innominata; Med., medial; Nucl., nucleus; Olf., olfactory; Perf., perforated; Post., posterior; Subst., substance, substantia; Tuberc., tubercle; Uncin., uncinate.*

3.12-4.00 mm) deep to the subcallosal cortex bordering the interhemispheric fissure.

Cortical Gray Matter Relationships

The cortical areas found in this study to connect with or overlie the NAc and that constitute important networks with the NAc are the anterior cingulate cortex (BA 24), the dorsal and ventral parts of the paracingulate cortex (BA 32), and the subcallosal cortex (BA 25), in addition to the more inferiorly located prefrontal cortex, gyrus rectus, and medial orbitofrontal area (BA 11) in agreement with prefrontal compartmentalization of Ongür et al[18,19] (Figure 5). The anterior cingulate cortex has dorsal, ventral, and subgenual parts. The dorsal part is located above, the ventral part in front of, and the subgenual part below the genu of the corpus callosum. The paracingulate cortex (BA 32) has a dorsal portion located anterior to the genu of the corpus callosum and anterior cingulate cortex, and a ventral portion located below the subcallosal cortex and superior to the upturned posterior end of the gyrus rectus. The subcallosal cortex (BA 25), a small area directly anterior to the anterior commissure corresponding to the paraterminal gyrus, is located posterior to the subgenual anterior cingulate cortex and superior to the ventral paracingulate cortex. The prefrontal cortex constitutes an extensive area in front of the dorsal and ventral paracingulate cortex and above the gyrus rectus and medial orbitofrontal area. The gyrus


A
Sup. Lim. Sulc.
Ant. Lim. Sulc.
Caud. Head
Nucl. Acc.
Ant. Comm.
Ant. Crus
Int. Caps.
Inf. Lim. Sulc.
Glob. Pall.
Ant. Comm.
Post. Crus
Subst. Innom.
B
Cor. Rad.
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Int. Caps.
Ant. Limb
Ant. Comm.
Ant. Crus
Subst. Innom.
Ant. Comm.
Post. Crus
C
Stria Term.
Ant. Lim. Sulc.
Caud. Head
Nucl. Acc.
Ant. Comm.
Ant. Crus
Subst. Innom.
Caud. Tail
Ant. Comm.
Post. Crus
Inf. Lim. Sulc.
Meyer's Loop
D
Call. Fibers
Forceps Minor
Uncin. Fasc.
Nucl. Acc.
Ant. Comm.
Ant. Crus
Subthal. Nucl.
Ant. Comm. Body
Hypothal.
Caud. Tail
Ant. Comm.
Post. Crus
E
Stria Term.
Ext. Caps.
Extr. Caps.
Putamen
Ins. Cortex
Glob. Pall.
Stria Term.
Mam. Body
Caud. Tail
Hypothal.
Caud. Body
Fornix
Ant. Comm. Body
Caud. Head
Nucl.
Acc.
F
Caud. Head
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Ant. Comm. Body
Nucl. Acc.
Mam. Body
G
Call. Fibers
Forceps Minor
Nucl. Acc.
Uncin. Fasc.
Ant. Comm.
Ant. Crus
Subst. Innom.
Ant. Comm.
Post. Crus
Ant. Comm. Body
H
Ins. Cortex
Ant. Comm.
Ant. Crus
Putamen
Nucl. Acc.
Amyg.
Ant. Comm.
Post. Crus
Diag. Band
Uncin. Fasc.
Nucl. Acc.
Med. Olf. Stria
Ant. Comm. Body
Optic Fibers
Hippo.

FIGURE 2. *Location of the NAc.* **A**, *lateral view. Left hemisphere. The insular cortex, extreme and external capsules, claustrum, and putamen have been removed to expose the basal forebrain, globus pallidus, and internal capsule. The anterior, superior, and inferior insular limiting sulci have been preserved. The NAc is located below the head of the caudate nucleus, medial to the substantia innominata and anterior to the hypothalamus and blends without clear demarcation into all 3 structures. The anterior commissure has an anterior crus that projects forward toward the orbitofrontal area and a posterior crus that extends laterally along the base of the putamen. The anterior crus passes forward at the upper edge of the border between the NAc and substantia innominata.* **B**, *enlarged view. Removal of the putamen exposes the globus pallidus and anterior and posterior crura of the anterior commissure. The inferior edge of the anterior limb of the internal capsule courses directly above the anterior crus of the anterior commissure at the upper edge of the junction between the NAc and substantia innominata.[9,10]* **C**, *the globus pallidus and ventral part of the head of the caudate nucleus have been removed to better expose the NAc. The NAc is located below and anterior to the body and medial to the anterior crus of the anterior commissure.* **D**, *the majority of the left hemisphere and medial surface of the right hemisphere have been removed to expose the NAc bilaterally. The NAcs are positioned anteroinferior to the body of the anterior commissure. The lower part of the contralateral head of the caudate nucleus has been removed to expose the contralateral NAc.* **E**, *medial surface of left hemisphere. The caudate nucleus is an arched C-shaped structure that wraps around the thalamus in the lateral wall of the lateral ventricle. It has a head, body, and tail. The stria terminalis courses along the border between the caudate nucleus and thalamus. The NAc is located below the head of the caudate nucleus and anteroinferior to the upper edge of the body of the anterior commissure. The* **yellow dashed line** *outlines the NAc. The structures in the central core of the left hemisphere have been exposed from the medial side. The left lentiform nucleus, composed of the putamen laterally and globus pallidus medially, has also been exposed.* **F**, *enlarged view of (***E***).* **G**, *superior view. The NAc is located anteroinferior to the body and inferomedial to the anterior crus of the anterior commissure. The substantia innominata is positioned lateral to the NAc and inferolateral to the anterior crus of the anterior commissure. Callosal fibers (forceps minor) connect both prefrontal areas and the anteromedial surfaces of the paired NAcs. The uncinate fasciculus passes along the inferolateral surface of the NAc.* **H**, *inferior view. The fibers of the uncinate fasciculus passing below the NAc have been removed to expose the nucleus from below. The posterior part of the right olfactory nerve has been removed. The body of the anterior commissure crosses the posterosuperior edge of the paired NAcs. The medial olfactory stria and diagonal band of Broca cross the posteroinferior surface of the NAcs. Acc., accumbens; Amyg., amygdala; Ant., anterior; Call., callosal; Caps., capsule; Caud., caudate; Comm., commissure; Cor., corona; Diag., diagonal; Ext., external; Extr., extreme; Fasc., fasciculus; Glob., globus; Hippo., hippocampus; Hypothal., hypothalamus; Inf., inferior; Innom., innominata; Ins., insular; Int., internal; Lim., limiting; Mam., mammillary; Med., medial; Nucl., nucleus; Olf., olfactory; Pall., pallidus; Post., posterior; Rad., radiata; Subst., substantia; Subthal., subthalamic; Sulc., sulcus; Sup., superior; Term., terminalis; Uncin., uncinate.*

rectus (BA 14) is located anterior and inferior to the ventral paracingulate cortex and below the posterior one-third of the prefrontal cortex. The medial orbitofrontal area (BA 11) is located anterior to the gyrus rectus. The fibers underlying the dorsal paracingulate and subgenual anterior cingulate cortices are the cingulum and forceps minor, and those underlying the subcallosal cortex are the cingulum, forceps minor, indusium griseum, diagonal band of Broca, and a part of the uncinate fasciculus.

Functionally, the subcallosal and the subgenual anterior cingulate cortices constitute an important relay in a network that includes the cerebral cortex, limbic system, thalamus, hypothalamus, and brainstem nuclei.[20] Electrophysiological animal studies reveal that the subcortical projections from the subcallosal cortex connect to the inferomedial aspects of the head of the caudate nucleus, the periphery of the NAc, the bed nucleus of the stria terminalis, and the diagonal band of Broca and run caudally through the substantia innominata to reach the amygdala and hypothalamus.[20] The connections of the subcallosal cortex with the amygdala and orbitofrontal cortex are through the ventromedial part of the uncinate fasciculus. In addition, the ventromedial part of the uncinate fasciculus also connects the NAc with the temporal pole. These complex corticosubcortical connections involving the NAc are thought to form the emotional part of the limbic system involved in appreciation of pleasantness or unpleasantness of stimuli.[3,18]

Subcortical Gray Matter Relationships

The subcortical gray matter related to the NAc includes the septal nuclei, substantia innominata, caudate nucleus, hypothalamus, and indusium griseum. There is no clear demarcation between the caudate head, the substantia innominata, and the hypothalamus. The connections between these 3 masses of gray matter cannot be defined by a fiber dissection technique.

The septal region is located below the rostrum of the corpus callosum, anterosuperior to the body of the anterior commissure, anterior to the lamina terminalis and bed nucleus of the stria terminalis, and deep to the subcallosal cortex.[21] The septal region is composed of the medial septal complex, which includes the dorsally situated medial septal nucleus and the dorsal limb of the nucleus of the diagonal band of Broca. The NAc is positioned ventrolateral to the septal region and has documented electrophysiological connections with the septal nuclei.[22,23] The ventral limb of the nucleus of the diagonal band extends into the fibers of the diagonal band, which pass caudolaterally along the ventral surface of the hemisphere at the caudal edge of the olfactory tubercle (Figure 2H and 6F).

The medial septal complex connects with all parts of the hippocampus, including the subiculum and the entorhinal cortex, and all parts of the hypothalamus.[24] Given the topographical organization of the septohippocampal and septohypothalamic connections, it seems likely that specific hippocampal domains selectively influence particular motivated behaviors, such that lesions of the septal region may lead to marked changes in ingestive, sexual, and antagonistic behavior.[24]

The substantia innominata, an ill-defined mass of gray matter below the anterior part of the putamen, is positioned lateral to the NAc and hypothalamus, above the anterior perforated

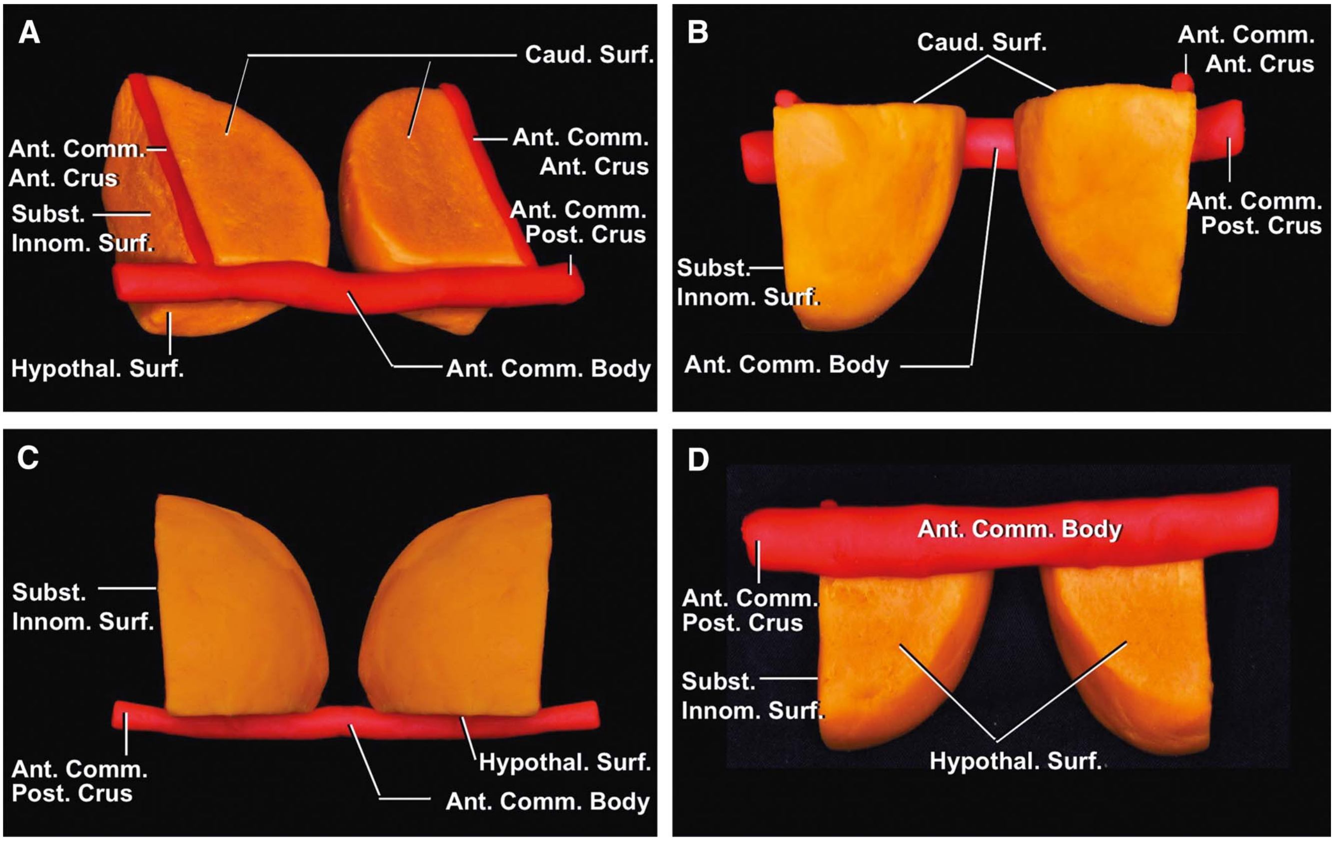


FIGURE 3. *Relationship of the NAc and anterior commissure.* **A**, *oblique right posterosuperior view.* **B**, *anterior view.* **C**, *inferior view.* **D**, *posterior view.* **A-D**, *the anterior commissure has a body that crosses the midline and the posterosuperior edge of the NAc. The superior surface of the NAc blends into the head of the caudate, the lateral surface into the substantia innominata, and the posterior surface into the hypothalamus. The body of the anterior commissure has an anterior crus that crosses the superolateral edge of the NAc and a posterior crus that extends laterally to the temporal lobe. Ant., anterior; Caud., caudate; Comm., commissure; Hypothal., hypothalamus; Post., posterior; Subst. Innom., substantia innominata; Surf., surface.*

substance, and anterior to the posterior crus of the anterior commissure (Figures 1 and 2).[21] The substantia innominata is continuous superomedially with the bed nucleus of the stria terminalis and blends inferolaterally into the amygdaloid complex. In our fiber dissections, there was no clear demarcation between the NAc and the remaining parts of the substantia innominata and septal nucleus. However, the inferior edge of the anterior limb of the internal capsule and adjacent anterior crus of the anterior commissure are considered to form the boundary between the NAc and the substantia innominata.[11,12] The substantia innominata also includes an extension to the amygdala that links it with the bed nucleus of the stria terminalis, called the extended amygdala, and the basal nucleus of Meynert, a poorly defined part of the substantia innominata lateral to the NAc.[4,25]

The indusium griseum is a thin, grayish, sheetlike remnant of the hippocampus that continues around the corpus callosum as small, paired, mixed gray and white matter tracts, the medial and lateral longitudinal striae, that, with the diagonal band, form the paraterminal gyrus and blend into the superomedial side of the NAc (Figures 6E and 6F).[26,27]

Connections of the NAc

The fiber pathways passing adjacent to and connecting to the NAc were the uncinate fasciculus, cingulum, stria medullaris thalami, fornix, diagonal band of Broca, stria terminalis, medial olfactory stria, and forceps minor (Figure 7). These 8 tracts form a capsule around the anterior, inferior, and medial sides of the NAc. The uncinate fasciculus connects along the inferior and adjacent part of the medial side of the NAc, the cingulum and diagonal band along the medial surface, the medial olfactory stria along the inferomedial and posterior part of the medial surface, the forceps minor along the anteromedial surface, and the stria terminalis, fornix, and stria medullaris along the posterosuperior surface. The diagonal band of Broca and medial

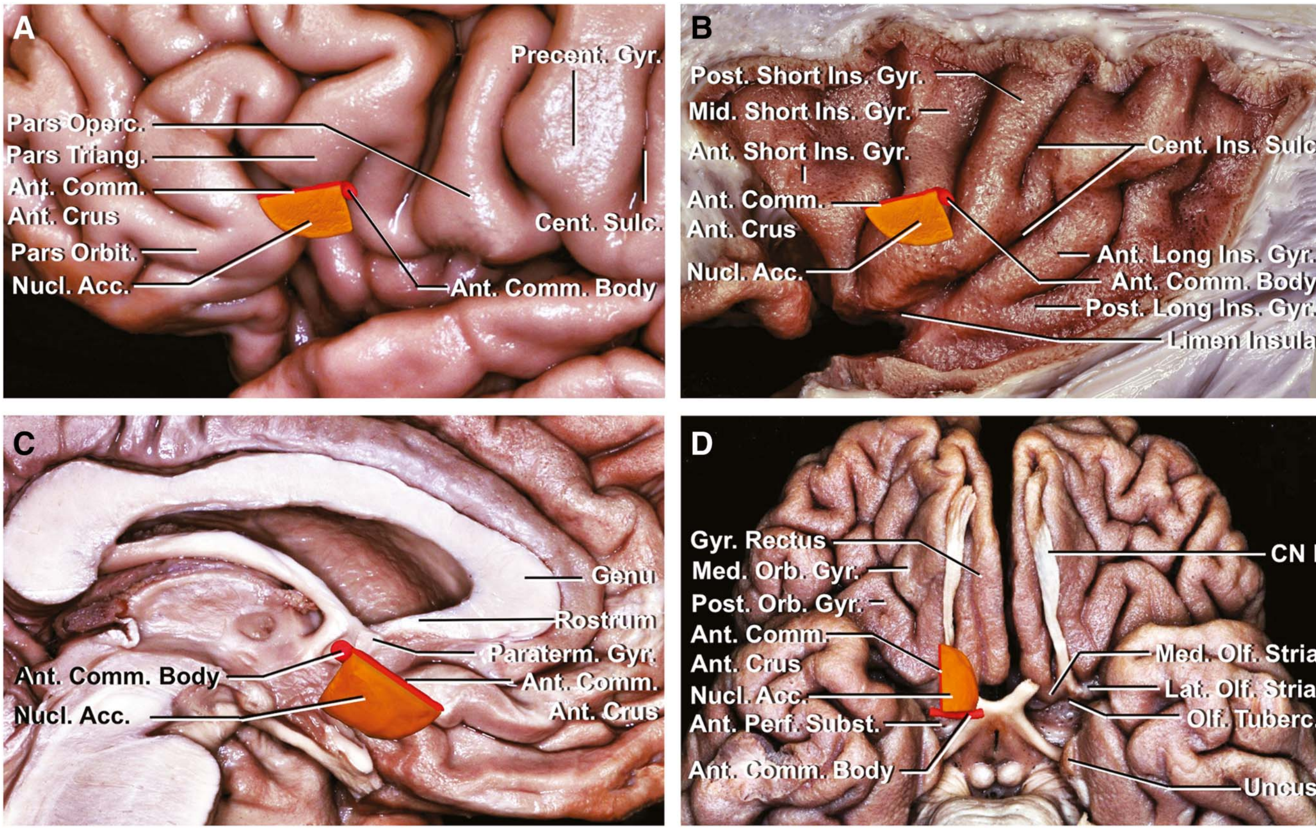


FIGURE 4. *The NAc in relation to surface landmarks.* **A**, *lateral surface. Left hemisphere. The NAc is shown in* **orange**, *and the anterior commissure in* **red**. *The NAc is positioned deep to the lower half of the pars triangularis on the inferior frontal gyrus.* **B**, *lateral surface. The NAc is positioned deep to the lower half of the anterior and middle short insular gyri.* **C**, *medial surface. The NAc is positioned lateral to the area of the paraterminal gyrus, lower half of the subcallosal cortex, and the ventral paracingulate cortex.* **D**, *inferior surface. The NAc is positioned just above the posterior part of the gyrus rectus and anteromedial part of the anterior perforated substance. Acc., accumbens; Ant., anterior; Cent., central; CN, cranial nerve; Comm., commissure; Gyr., gyrus; Ins., insular; Lat., lateral; Med., medial; Mid., middle; Nucl., nucleus; Olf., olfactory; Operc., opercularis; Orb., orbital; Orbit., orbitalis; Paraterm., paraterminal; Perf., perforated; Post., posterior; Precent., precentral; Subst., substance; Sulc., sulcus; Triang., triangularis; Tuberc., tubercle.*

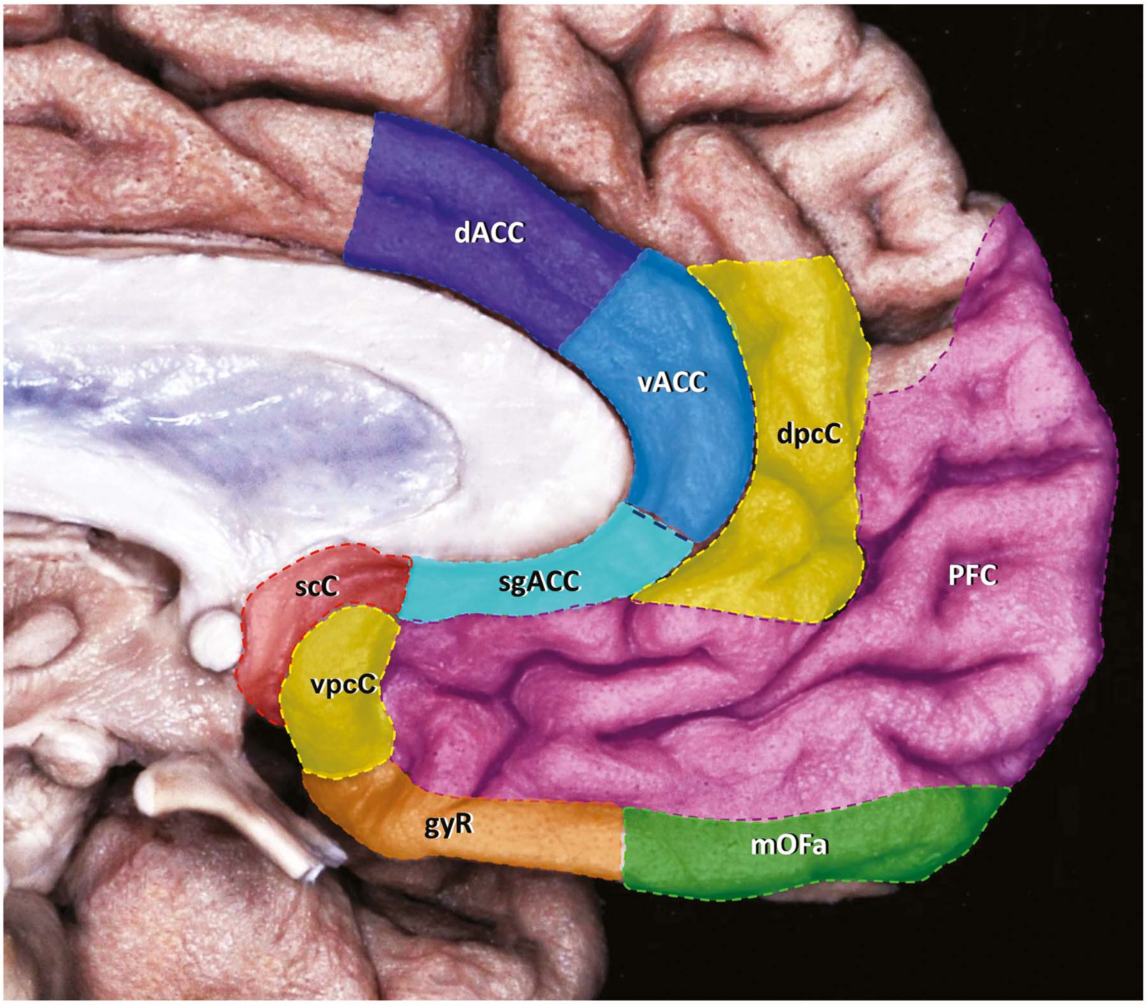
olfactory stria course posterior to the cingulum and uncinate fasciculus (Figure 7).

Uncinate Fasciculus

The uncinate fasciculus is a long association pathway that connects the frontal and temporal regions and has a hook-shaped course deep to the limen insulae (Figures 6A-6D, 7, 8F, 8I, and 8J). It has 2 parts: ventromedial and anterolateral, as proposed by Ebeling and von Cramon.[28] In our dissections, the ventromedial part connected the orbital surface of the frontal lobe, septal area, NAc, and medial orbitofrontal area to the amygdala and parahippocampal gyrus. It passed anterior to the anterior perforated substance and covered the inferior and medial surfaces of the NAc. The anterolateral part connected the superolateral part of the frontal lobe and the lateral temporal gyri near the temporal pole.

Tracing studies in monkeys have shown that the NAc receives afferent fibers from structures associated with the limbic system, including the medial orbitomedial area, amygdala, anterior cingulate cortex, and temporal pole, most likely through the uncinate fasciculus.[22] The ventromedial fibers also interconnect posterior aspects of the subcallosal cortex (BA 25) and the amygdala. The uncinate fasciculus, a part of the ventral limbic pathway, comes together with the cingulum, the dorsal limbic pathway, within the subcallosal cortex on the medial surface of the NAc.[29,30]

Connections take 2 routes from the ventral striatum to the medial temporal lobe. One is laterally through the uncinate fasciculus to the amygdala, and the other is along the stria terminalis. The former route also carries amygdalar inputs to medial prefrontal and adjacent orbitofrontal areas via the uncinate fasciculus and could provide part of the anatomic substrate for the altered amygdala–ventral striatum interactions in depression, and a role in the appreciation of the emotional significance of stimuli and generation of emotional



	Related Tracts
dACC: Dorsal anterior cingulate cortex	Cingulum, Indusium griseum
vACC: Ventral anterior cingulate cortex	Cingulum, Indusium griseum
sgACC: Subgenual anterior cingulate cortex	Cingulum, Indusium griseum, Forceps minor
scC: Subcallosal cortex	Cingulum, Indusium griseum, Forceps minor, Diagonal band of Broca, Uncinate fasciculus
dpcC: Dorsal paracingulate cortex	Cingulum, Forceps minor
vpcC: Ventral paracingulate cortex	Cingulum, Forceps minor, Uncinate fasciculus
PFC: Prefrontal cortex	Cingulum, Forceps minor, Uncinate fasciculus
gyR: Gyrus rectus	Uncinate fasciculus
mOFa: Medial orbitofrontal area	Uncinate fasciculus

FIGURE 5. *Medial surface of the frontal lobe showing the cortical areas related to the nucleus accumbens (NAc). The fiber tracts NAc-connected fiber tracts underlying each related cortical area connecting to the NAc are listed below the illustration according to which related cortical area they lie beneath. The anterior cingulate cortex (BA 24), which has 3 parts, dorsal, ventral, and subgenual, wraps around the anterior part of the body and the genu of the corpus callosum. The subcallosal cortex (BA 25) is located below the rostrum of the corpus callosum and posterior to the subgenual anterior cingulate cortex. The subcallosal cortex includes the paraterminal gyrus. The anterior cingulate (BA 24), subcallosal (BA 25), and dorsal and ventral paracingulate (BA 32) cortices connect to the NAc, mainly through the cingulum. The paracingulate cortex (BA 32) has a dorsal portion located in the classic paracingulate region, anterior to the corpus callosum, and a ventral portion located below the subcallosal cortex. The gyrus rectus (BA 14) is located anterior and inferior to the ventral paracingulate gyrus. The medial orbitofrontal area (BA 11) is located anterior to the gyrus rectus. The uncinate fasciculus courses deep to the gyrus rectus (BA 14) and medial orbitofrontal area (BA 11) to connect to the NAc. BA, Brodmann area.*

expression.[20] It should be emphasized that the uncinate fasciculus is not the only connection between the amygdala and the NAc. Information can flow via the ventral amygdalofugal pathway (stria terminalis) to the NAc and from the central amygdaloid nuclei via the connection at the extended amygdala.[24]

Cingulum

In our dissections, the cingulum, the long association pathway running within the cingulate gyrus, connected the hippocampal formation, entorhinal cortex, and parahippocampal gyrus to the subgenual anterior cingulate and subcallosal cortices, paraterminal gyrus, septal area, and NAc (Figures 6E, 6F, 7, 8E, 8F). The cingulum, after passing through the subgenual anterior cingulate cortex (BA 24), connects to the medial part of the NAc. In our medial to lateral dissections, the cingulum and the ventromedial fibers of the uncinate fasciculus join in the subcallosal and paracingulate cortices and the posterior part of the prefrontal cortex, referred to as the cingulate pole by Yaşargil.[30]

According to Dejerine,[31] the cingulum is not formed by fibers that travel the whole length of the fascicle, but by short fibers that arise in the neighboring gyri along its path. Dejerine also observed that the cingulum receives fibers not only from the superior frontal gyrus, but also from the paracentral lobule, precuneus, cuneus, lingual gyrus, and even the temporal pole.[29,31,32] Tracing studies in animals demonstrated the link between the cingulum and ventral striatum and also that lesions of the prefrontal cortex led to degeneration of fibers in the cingulum that reach the presubicula and entorhinal area of the medial temporal lobe.[29] Several studies revealed that there is clear intermixing of the cingulum with the uncinate fasciculus at the subcallosal cortex.[29,33]

In a recent review of the practical considerations in the refinement of subcallosal cingulate white matter DBS for depression, Riva-Posse et al[34] emphasized the controversy regarding the existing neuroanatomic terminology of the subcallosal region among clinical studies, including the subcallosal cortex (BA 25), ventral paracingulate cortex (BA 32), and the posterior part of the prefrontal cortex (BA 10). The authors clearly pinpoint the area of conflict, which also includes the anatomic boundaries defining the subcallosal cortex (BA 25) from adjacent BA 32, BA 24, and the posterior part of the prefrontal cortex. This review fairly delineated the area of conflict by adhering to the Ongür et al[19] classification and using the sagittal plane on magnetic resonance images. Our study used the same nomenclature and proposed cortical boundaries as Riva-Posse et al[34] to define the complex white matter connections of the area.

Long-term DBS of the cingulum at the level of the subcallosal cortex (BA 25, subcallosal cingulate cortex) and the ventral striatum have been investigated for patients with treatment-resistant depression and both have shown promise, without Class I evidence to support them thus far.[34,35] Notably, recent work in particular supports the subcallosal cortex (BA 25) as the relevant target over ventral striatum.[36,37] Heilbronner and Haber,[38] using tract-tracing techniques, have illustrated the route and composition of the cingulate bundle and discussed the effects of DBS with regard to neighboring white matter tracts and their cortical extensions. These authors argued that the electrode, located in the caudal portion of the subgenual part of the cingulate bundle, will likely affect both subcortical and cortical fibers in the cingulum, along with ventral prefrontal cortical fibers in the nearby uncinate fasciculus.[38] According to their observations in nonhuman primates, Heilbronner and Haber[38] proposed that the subcallosal DBS will also capture amygdala pathways as they travel via the subgenual cingulum. In this vein, Lujan et al[35] considered the widespread network changes associated with DBS induced antidepressant effects through neuroimaging and highlighted the low probability of a single axonal pathway accounting for all of the therapeutic effects of the treatment modality. However, the most likely explanation of the therapeutic effect is the stimulation of the part of the cingulum connecting the subcallosal cortex and the NAc, rather than its connections to the amygdala, hypothalamus, and orbitofrontal cortex.[35] We believe that the link between the cingulum and the ventral striatum provided by the NAc can best be appreciated through fiber dissections of the human brain, since experimental studies tend to underrate this relationship.[22,39,40] The fibers emanating from the paracentral lobule and precuneus also joined the cingulum on its way to the subcallosal cortex.[32,41]

Papez[42] proposed in 1937 that the cingulum was an integral component of the emotion circuit, and MacLean[43] included the bundle in his conception of the "visceral brain" in 1949. The fibers passing through the cingulum are linked with striatal regions, including the ventral striatum, and thus may play a role in initiating the expression of affective behavior, control of emotions, and response to specific impulses.[24,29,31]

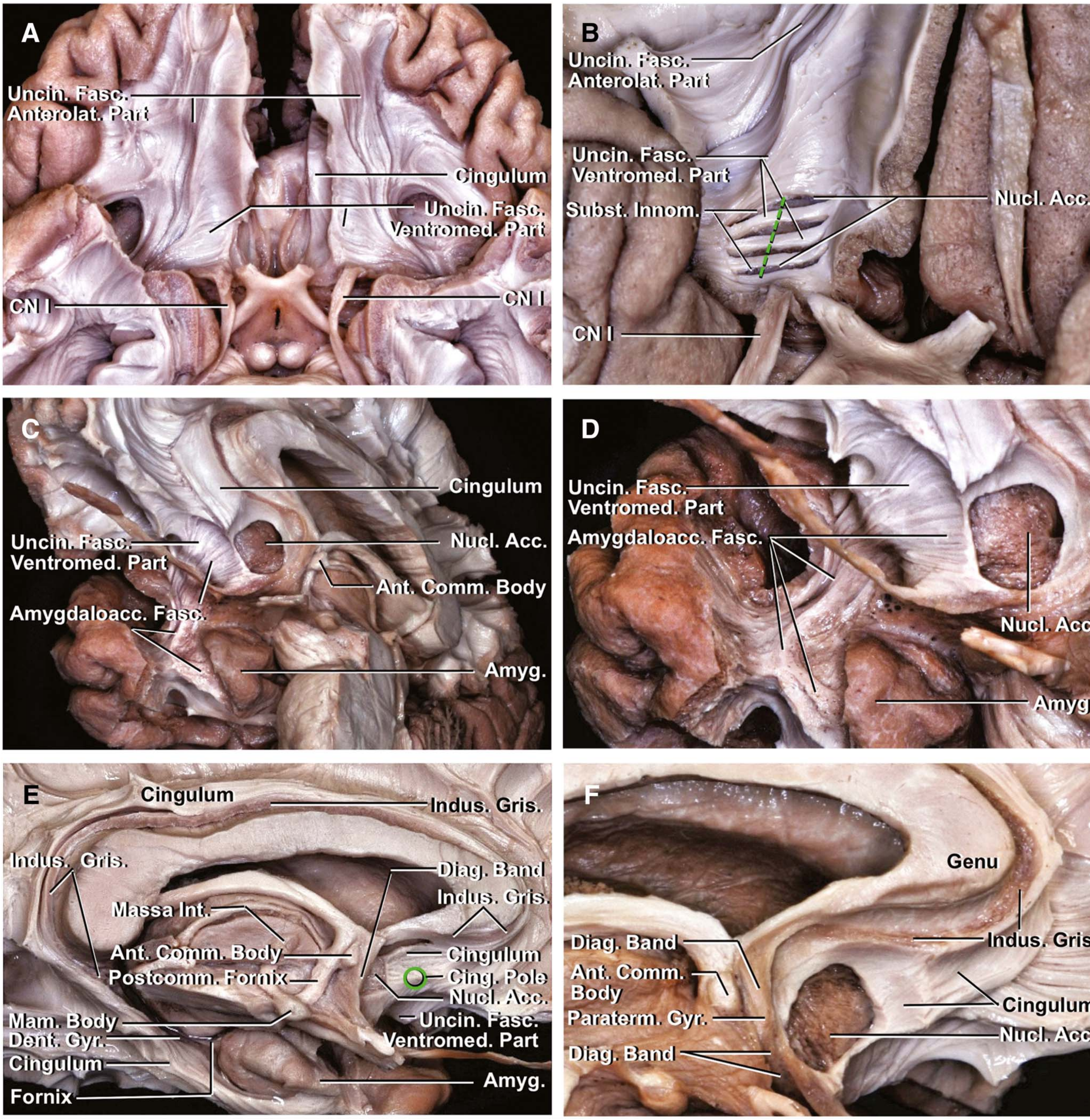

A
Uncin. Fasc.
Anterolat. Part
Cingulum
Uncin. Fasc.
Ventromed. Part
CN I
CN I
B
Uncin. Fasc.
Anterolat. Part
Uncin. Fasc.
Ventromed. Part
Subst. Innom.
Nucl. Acc.
CN I
C
Cingulum
Uncin. Fasc.
Ventromed. Part
Nucl. Acc.
Ant. Comm. Body
Amygdaloacc. Fasc.
Amyg.
D
Uncin. Fasc.
Ventromed. Part
Amygdaloacc. Fasc.
Nucl. Acc.
Amyg.
E
Cingulum
Indus. Gris.
Indus. Gris.
Diag. Band
Indus. Gris.
Massa Int.
Ant. Comm. Body
Cingulum
Postcomm. Fornix
Cing. Pole
Nucl. Acc.
Mam. Body
Uncin. Fasc.
Dent. Gyr.
Ventromed. Part
Cingulum
Amyg.
Fornix
F
Genu
Diag. Band
Indus. Gris.
Ant. Comm.
Body
Cingulum
Paraterm. Gyr.
Nucl. Acc.
Diag. Band

FIGURE 6. *Connections of the NAc. A, inferior view. The cortex forming the medial part of the basal surface of the frontal lobe formed by the orbital gyri and the gyrus rectus has been removed to expose the uncinate fasciculus. The uncinate fasciculus crossing the basal surface of the frontal lobe is divided into an anterolateral part, which projects to the lateral orbitofrontal area, and a ventromedial part, which projects to the medial orbitofrontal and septal areas. The ventromedial part of the uncinate fasciculus connects the NAc to the temporal lobe and orbitofrontal areas. The olfactory nerves were reflected posteriorly to improve the exposure. B, another specimen. Some fascicles of the ventromedial part of the right uncinate fasciculus have been peeled away to expose the NAc and adjacent substantia innominata. The ventromedial part of the right uncinate fasciculus crosses the inferior and medial surfaces of the NAc. The anterior crus of the anterior commissure, which passes above the* **dashed green lines***, forms the border between the NAc medially and the substantia innominata laterally. C, inferomedial oblique view of the medial surface of the right hemisphere. Some cingulum fibers have been removed to expose the NAc. The amygdala in the right anteromedial temporal lobe has been exposed. The fibers of the ventromedial part of the uncinate fasciculus that connects the amygdala to the NAc are also referred to as the amygdaloaccumbens fasciculus. D, enlarged view of (C). E, medial surface, left hemisphere. The cingulum, a fiber tract underlying the cingulate cortex, originates in the entorhinal cortex and anterior part of the parahippocampus, and terminates in the subgenual anterior cingulate and subcallosal cortices and paraterminal gyrus. The cingulum covers the medial surface of the NAc. Some fibers from the medial frontal gyri, paracentral lobule, and precuneus and cuneus join the cingulum. The uncinate fasciculus, the ventral limbic pathway, and cingulum, the dorsal limbic pathway meet at the area along the medial and inferior surfaces of the NAc, called the cingulate pole (***green circle***). The indusium griseum and diagonal band meet to form the paraterminal gyrus. The indusium griseum can be followed backward around the splenium to reach the dentate gyrus. F, another specimen, enlarged view. The cortex, fibers of the cingulum, and the ventromedial part of the uncinate fasciculus have been removed to expose the NAc. The indusium griseum and diagonal band of Broca meet at the paraterminal gyrus located along the posteromedial edge of the NAc. Acc., accumbens; Amyg., amygdala; Amygdaloacc., amygdaloaccumbens; Ant., anterior; Anterolat., anterolateral; Cing., cingulate; CN, cranial nerve; Comm., commissure; Dent., dentate; Diag., diagonal; Fasc., fasciculus; Gyr., gyrus; Indus. Gris., indusium griseum; Int., intermedia; Mam., mammillary; Nucl., nucleus; Paraterm., paraterminal; Postcomm., postcommissural; Subst. Innom., substantia innominata; Uncin., uncinate; Ventromed., ventromedial.*

The main efferent output of the NAc projects to the cingulate cortex, ventral pallidum, and thalamus.[44,45] The interconnections found in this study provide further anatomic support for the use of DBS in this region for the treatment of neuropsychiatric disorders, particularly drug-resistant depression, OCD, and addiction.[1,8,29,46] Cingulotomy, as an alternative to standard prefrontal leucotomy/lobotomy, was introduced for depression and psychosis based on the theory of Papez and on observations in the monkey demonstrating tameness and loss of fear after ablation of the anterior cingulate cortex.[47,48] However, cingulotomy, most commonly used for OCD and chronic pain disorders in recent years, has also been introduced for other conditions such as depression, drug addiction, and aggressiveness.[5,49-54] It has been suggested that extensive disconnection among various cortical, subcortical, and limbic structures could be achieved by disrupting the cingulum because of its heterogeneous composition.[42] Bilateral stereotactic cingulotomy has also been performed for OCD.[55]

Stria Medullaris Thalami

Our dissections revealed that the stria medullaris thalami connects the septal and preopticohypothalamic areas to the habenula (Figures 7, 8A, 8B, and 8D). The stria medullaris passes along the taenia thalami, a strip of nervous tissue on the dorsomedial surface of the thalamus directly adjacent to the line of attachment of the membranous roof of the third ventricle. The stria medullaris thalami blends into the posterosuperior edge of the NAc adjacent to the body of the anterior commissure.

The habenular complex is a small mass of gray matter medial to the caudal part of the thalamus directly beneath the diencephalic ventricular surface.[24] The habenula receives afferents via the stria medullaris thalami and gives origin to the habenulointerpeduncular tract (fasciculus retroflexus). The medial and lateral habenular nuclei receive their afferents principally from the nuclei of the diagonal band, the medial septal complex, substantia innominata, and lateral preopticohypothalamic area.[24] It has been proposed that the striae medullaris carries afferents from the NAc to the habenula that may be involved in stress responses and sleep-wake cycles.[24]

Fornix

The fornix, an efferent pathway of the hippocampus, connects the hippocampal formation to the septal area and hypothalamus (Figures 7, 8A, and 8B).[24,56] The fornix arises in the hippocampal formation and, at the level of the body of the fornix, divides into columns, which form the superior and anterior edges of the foramen of Monro. The columns of the fornix divide into precommissural and postcommissural parts at the level of the body of the anterior commissure. In our dissections the precommissural fornix could be followed into the posterosuperior part of the NAc beside the septal area, as noted by others.[23,32,56,57] The postcommissural fornix descends to reach the mammillary body.

The fornix connects the hippocampus to the medial septal/diagonal band complex.[24] Electrophysiological studies in animals have shown that signals from the hippocampus reach the medial prefrontal areas and the subpallidal regions via the fornix, NAc, and hippocampoprefrontal/hippocamposubpallidal networks.[23,57] The projections from adjacent medial prefrontal and orbitofrontal areas traveling via the fornix, by way of the NAc, to the hippocampus also provide another network for altered hippocampal–subgenual anterior cingulate cortex interactions in mental disorders.[34,58]

Diagonal Band of Broca

In our dissections, the diagonal band passed along the medial surface of the NAc posterior to the medial olfactory stria, cingulum, and uncinate fasciculus (Figures 7, 8C, and 8F). This amygdalofugal pathway is divided into a ventral part called the ansa peduncularis and a dorsal part called the stria terminalis. The ansa peduncularis is further divided into the diagonal band (amygdaloseptal pathway), medial forebrain bundle (amygdalohypothalamic), and inferior thalamic peduncle (amygdalothalamic).[24,59] The diagonal band courses medially after leaving the ansa peduncularis to reach the medial side of the NAc. The

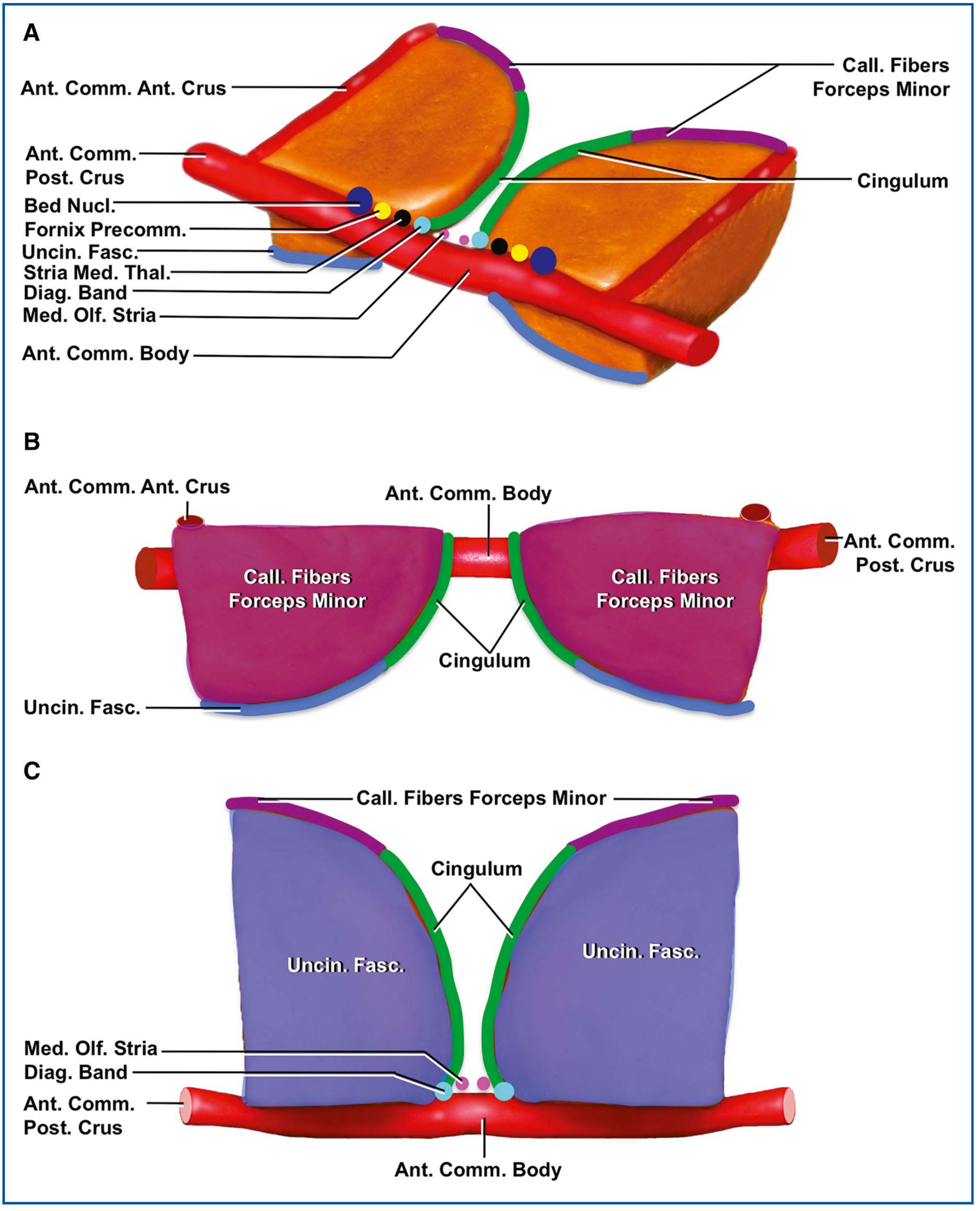

A
Ant. Comm. Ant. Crus
Ant. Comm.
Post. Crus
Bed Nucl.
Fornix Precomm.
Uncin. Fasc.
Stria Med. Thal.
Diag. Band
Med. Olf. Stria
Ant. Comm. Body
Call. Fibers
Forceps Minor
Cingulum
B
Ant. Comm. Ant. Crus
Ant. Comm. Body
Ant. Comm.
Post. Crus
Call. Fibers
Forceps Minor
Call. Fibers
Forceps Minor
Cingulum
Uncin. Fasc.
C
Call. Fibers Forceps Minor
Cingulum
Uncin. Fasc.
Uncin. Fasc.
Med. Olf. Stria
Diag. Band
Ant. Comm.
Post. Crus
Ant. Comm. Body

FIGURE 7. *Connections of the nucleus accumbens (NAc).* **A**, *right posterolateral oblique view.* **B**, *anterior view.* **C**, *inferior view. Callosal fibers in the forceps minor connect along the anteromedial surface of the NAc, cingulum fibers along the medial surface, and uncinate fasciculus along the inferior and medial surface. The bed nucleus of the stria terminalis, precommissural fornix, and stria medullaris thalami connect along the medial part of the posterosuperior surface of the NAc. The diagonal band and medial olfactory stria connect along the superior part of the posteromedial surface of the NAc. The head of the caudate nucleus is positioned above the NAc, the substantia innominata lateral to the NAc, and the hypothalamus posterior to the NAc. The border between the NAc and the substantia innominata is located at the level of the anterior crus of the anterior commissure or the adjacent inferior edge of the anterior limb of the internal capsule. Ant., anterior; Call., callosal; Comm., commissure; Diag., diagonal; Fasc., fasciculus; Med., medial, medullaris; Nucl., nucleus; Olf., olfactory; Post., posterior; Precomm., precommissural; Thal., thalami; Uncin., uncinate.*

indusium griseum and diagonal band meet along the medial surface of the NAc to form the paraterminal gyrus.[56,59]

Stria Terminalis

In our dissections the stria terminalis followed a C-shaped course along the striathalamic sulcus, which separates the thalamus and caudate nucleus, to terminate in the bed nucleus of the stria terminalis and adjacent the NAc (Figures 7, 8E, 8G, and 8H). The stria terminalis, referred to as the dorsal amygdalofugal pathway, connects the amygdala to the hypothalamus and septal area.[24,56,60] Several lines of evidence support the concept that this amygdalostriatal projection arises from the basal nuclei of the amygdala and terminates mainly in the ventral striatum.[24] Double-labeling experiments in rats revealed that numerous neurons in the basolateral amygdaloid nucleus project to both the prefrontal cortex and NAc via the stria terminalis. Most of our knowledge about the bed nucleus of the stria terminalis and its structural connectivity comes from tracer studies in rodents showing that the bed nucleus has extensive connections to other limbic regions including the amygdala, hypothalamus, hippocampus, and especially the NAc and ventral tegmental area.[61] Studies on functional connectivity in humans and nonhuman primates demonstrated the close relationship between the bed nucleus of the stria terminalis and the central nucleus of the amygdala.[4,24] However, recent human diffusion tensor imaging and resting state functional MRI studies revealed that the strongest structural connection of the bed nucleus of the stria terminalis is with the NAc via the stria terminalis.[61] This connection between the bed nucleus of the stria terminalis and NAc is especially important because both structures have a prominent role in addiction neurocircuitry.[61,62]

Medial Olfactory Stria

In our inferior surface dissections, the olfactory tract divided into medial and lateral olfactory striae just anterior to the olfactory tubercle and coursed along the anterior edge of the anterior perforated substance (Figures 2H, 7, 8C, and 8F). The medial olfactory stria crossed the medial part of the anterior edge of the anterior perforated substance below the NAc and ascended along the posterior part of the medial surface of the NAc and anteroinferior part of the paraterminal gyrus. The medial olfactory stria does not receive any secondary olfactory fibers.[24] The entire secondary olfactory projection passes through the lateral olfactory stria to end in the prepiriform or periamygdaloid gyri or the semilunar gyrus of the anterior part of the medial temporal lobe.[24]

Forceps Minor

In our dissections, the fibers passing through the part of the genu of the corpus callosum referred to as the forceps minor course along the anteromedial surface of the NAc toward the frontal poles to connect to the prefrontal and medial orbitofrontal areas and the NAcs from side to side, as previously reported (Figures 2G, 2H, 7, 8I, and 8J).[24,29]

Dissection of the NAc Guided by Surgical Navigation System

In this study, structures encountered in passing a probe from Kocher's point, located 2 cm lateral to the midline and 2 cm anterior to the coronal suture, to the NAc were the SLF II, the corona radiata, and the head of the caudate nucleus (Figure 9). A 6 × 6-cm frontoparietal craniotomy around the probe was performed to allow dissection and identification of the fiber tracts along the advancing tip of the probe. Removal of the cortex and subcortical U-fibers exposed the SLF II in the frontoparietal region. Removing the SLF II exposed the vertically oriented corona radiata. Removal of the corona radiata exposed the head of the caudate nucleus located between the internal capsule and frontal horn of the lateral ventricle. Removal of the head of the caudate exposed the NAc, located anterior to the body of the anterior commissure. Each step was mapped with navigation coordinates. This trajectory, directed just lateral to the frontal horn and through the caudate nucleus, has been well tolerated in DBS for OCD and depression, as has the adjacent trajectory used for DBS of the globus pallidus in Parkinson disease.[41,63-65]

The pivotal functional role of the NAc as a motor limbic interface and its proximity to other neural regions give rise to concerns related to adverse effects related to stimulation of adjacent areas, such as cognitive impairment.[8] Some minor cognitive deficits, such as memory impairment, may be expected due to microtrauma to the head of the caudate, but patients without preoperative dementia are at lower risk.[66,67] Other nearby structures that might be damaged in targeting the NAc are the anterior cerebral artery and optic nerve.

DISCUSSION

The concept of the basal ganglia was extended by Heimer and Wilson,[4] who postulated that the caudate nucleus, putamen, and globus pallidus represent only the dorsal part of the striatal

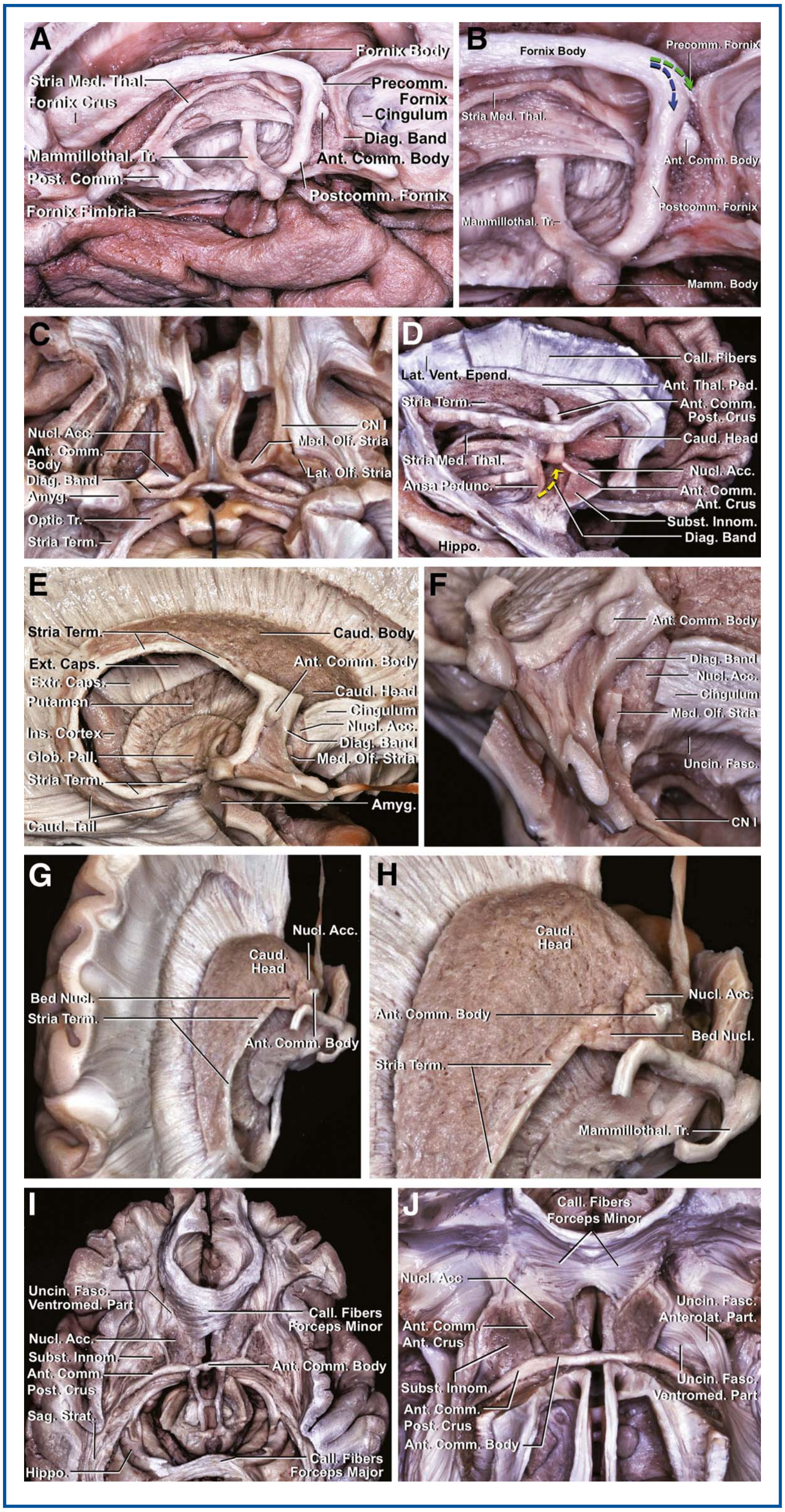

A
Fornix Body
Stria Med. Thal.
Fornix Crus
Precomm. Fornix
Cingulum
Diag. Band
Mammillothal. Tr.
Ant. Comm. Body
Post. Comm.
Postcomm. Fornix
Fornix Fimbria
B
Fornix Body
Precomm. Fornix
Stria Med. Thal.
Ant. Comm. Body
Postcomm. Fornix
Mammillothal. Tr.
Mamm. Body
C
Nucl. Acc.
Ant. Comm. Body
Diag. Band
Amyg.
Optic Tr.
Stria Term.
CN I
Med. Olf. Stria
Lat. Olf. Stria
D
Call. Fibers
Lat. Vent. Epend.
Ant. Thal. Ped.
Stria Term.
Ant. Comm. Post. Crus
Caud. Head
Stria Med. Thal.
Nucl. Acc.
Ansa Pedunc.
Ant. Comm. Ant. Crus
Subst. Innom.
Hippo.
Diag. Band
E
Stria Term.
Caud. Body
Ext. Caps.
Ant. Comm. Body
Extr. Caps.
Caud. Head
Putamen
Cingulum
Nucl. Acc.
Ins. Cortex
Diag. Band
Glob. Pall.
Med. Olf. Stria
Stria Term.
Amyg.
Caud. Tail
F
Ant. Comm. Body
Diag. Band
Nucl. Acc.
Cingulum
Med. Olf. Stria
Uncin. Fasc.
CN I
G
Nucl. Acc.
Caud. Head
Bed Nucl.
Stria Term.
Ant. Comm. Body
H
Caud. Head
Nucl. Acc.
Ant. Comm. Body
Bed Nucl.
Stria Term.
Mammillothal. Tr.
I
Uncin. Fasc. Ventromed. Part
Call. Fibers Forceps Minor
Nucl. Acc.
Subst. Innom.
Ant. Comm. Body
Ant. Comm. Post. Crus
Sag. Strat.
Call. Fibers Forceps Major
Hippo.
J
Call. Fibers Forceps Minor
Nucl. Acc.
Uncin. Fasc. Anterolat. Part.
Ant. Comm. Ant. Crus
Uncin. Fasc. Ventromed. Part
Subst. Innom.
Ant. Comm. Post. Crus
Ant. Comm. Body

FIGURE 8. *Connections of the nucleus accumbens (NAc).* **A**, *medial view, left hemisphere. The fimbria, crus, body, and columns of the fornix have been exposed. The body of the fornix divides into paired columns anterior to the foramen of Monro. The columns divide into a precommissural bundle terminating in the septal area and a postcommissural bundle terminating in the mammillary bodies. The mammillothalamic tracts connect the mammillary bodies to the anterior thalamic nuclei. The stria medullaris thalami connects the habenula to the preopticohypothalamic and septal regions.* **B**, *enlarged view. The* **dashed green line** *follows the smaller precommissural fornix, which ends in the septal region, and the* **dashed blue line** *follows the larger postcommissural fornix, which ends in the mammillary bodies.* **C**, *inferior view. The basal forebrain has been exposed from below. The diagonal band of Broca passes medially below and upward along the medial side of the NAc, in front of the optic tract and posterior and inferior to the body of the anterior commissure to reach the amygdala.* **D**, *lateral view, right hemisphere. The ipsilateral frontal, parietal, and occipital lobes have been removed. The posterior crus of the anterior commissure has been reflected upward to expose the ansa peduncularis. The paraterminal gyrus, formed by the indusium griseum, and the diagonal band (***dashed yellow line***), an amygdaloseptal connection that forms part of the ansa peduncularis, have been exposed.* **E**, *medial view. The diagonal band lies in front of the anterior commissure. The stria terminalis passes along the border between the caudate nucleus and thalamus and connects the amygdala to the bed nucleus of the stria terminalis located near the anterior commissure.* **F**, *enlarged view of* **E**. *The olfactory tract divides posteriorly into the medial and lateral olfactory stria at the anterior edge of the anterior perforated substance. The medial olfactory stria ascends along the medial surface of the NAc. The cingulum passes medial to and the ventromedial part of the uncinate fasciculus passes below the NAc.* **G**, *superior view, left caudate nucleus. The bed nucleus of the stria terminalis has been exposed at the posterosuperior edge of the NAc.* **H**, *enlarged view of* **G**. **I**, *superior view. The callosal fibers (forceps minor) connect the anteromedial surfaces of the paired NAcs. The ventromedial part of the uncinate fasciculus connects the NAc and medial orbitofrontal area. The NAc is located anteroinferior to the body and inferomedial to the anterior crus of the anterior commissure.* **J**, *another specimen, superior view. Enlarged view of the connections between the forceps minor and paired NAcs. The substantia innominata is positioned inferolateral to the anterior crus of the anterior commissure. Acc., accumbens; Amyg., amygdala; Ant., anterior; Anterolat., anterolateral; Call., callosal; Caps., capsule; Caud., caudate; CN, cranial nerve; Comm., commissure; Diag., diagonal; Epend., ependyma; Ext., external; Extr., extreme; Fasc., fasciculus; Glob. Pall., globus pallidus; Hippo., hippocampus; Ins., insular; Lat., lateral; Mamm., mammillary; Mammillothal., mammillothalamic; Med., medial, medullaris; Nucl., nucleus; Olf., olfactory; Ped., peduncle; Pedunc., peduncularis; Post., posterior; Postcomm., postcommissural; Precomm., precommissural; Sag. Strat., sagittal stratum; Subst. Innom., substantia innominata; Term., terminalis; Thal., thalami, thalamic; Tr., tract; Uncin., uncinate; Vent., ventricle; Ventromed., ventromedial.*

complex and that the NAc, the adjacent part of the head of the caudate nucleus, and the olfactory tubercle form the ventral striatum.[39,68-70] The dorsal striatal system is proposed to play a role in initiating motor activities stemming from cognitive activities, whereas the ventral striatum is involved in initiating movements in response to emotionally or motivationally powerful stimuli.

The ventral striatum receives input from the medial orbitofrontal prefrontal cortex, but not from the motor, premotor, or supplementary motor regions of the frontal cortex and minimal, if any, input from BAs 9 and 46.[4,39,69] The amygdala, the most widely recognized structure associated with emotional behavior, also projects extensively to the ventral striatum.[39]

The corticostriatal circuit, involved in human behavior, forms several parallel and functionally segregated loop systems.[3] These projections pass from the cerebral cortex to the basal ganglia and return to the cortex via the thalamus. A motor loop involves the motor and premotor cortices, an associative or cognitive loop involves the dorsolateral prefrontal cortex, and a limbic loop involves the orbital and medial prefrontal cortex. The limbic component of the ventral striatum, including the NAc, is connected with other parts of the limbic system including the orbitofrontal and anterior cingulate cortices, amygdala, temporal pole, and hippocampus.

The limbic loop of the corticostriatal circuit contains fibers that originate from the orbital and medial prefrontal cortices and course along the ventral striatum (NAc) to reach the ventral pallidum.[71] These fibers leave the ventral pallidum, an extension of the globus pallidus located below the anterior commissure, and reach the mediodorsal thalamic nucleus. Information in the mediodorsal thalamic nucleus is then transmitted to the prefrontal cortex. This circuit is known as the corticostriatothalamocortical limbic loop (Figure 10).[18,19,71] The connection of the NAc to the gyrus rectus and medial orbitofrontal prefrontal cortex is through the uncinate fasciculus. Information conveyed between the ventral pallidum and mediodorsal thalamic nucleus is transmitted through the inferior

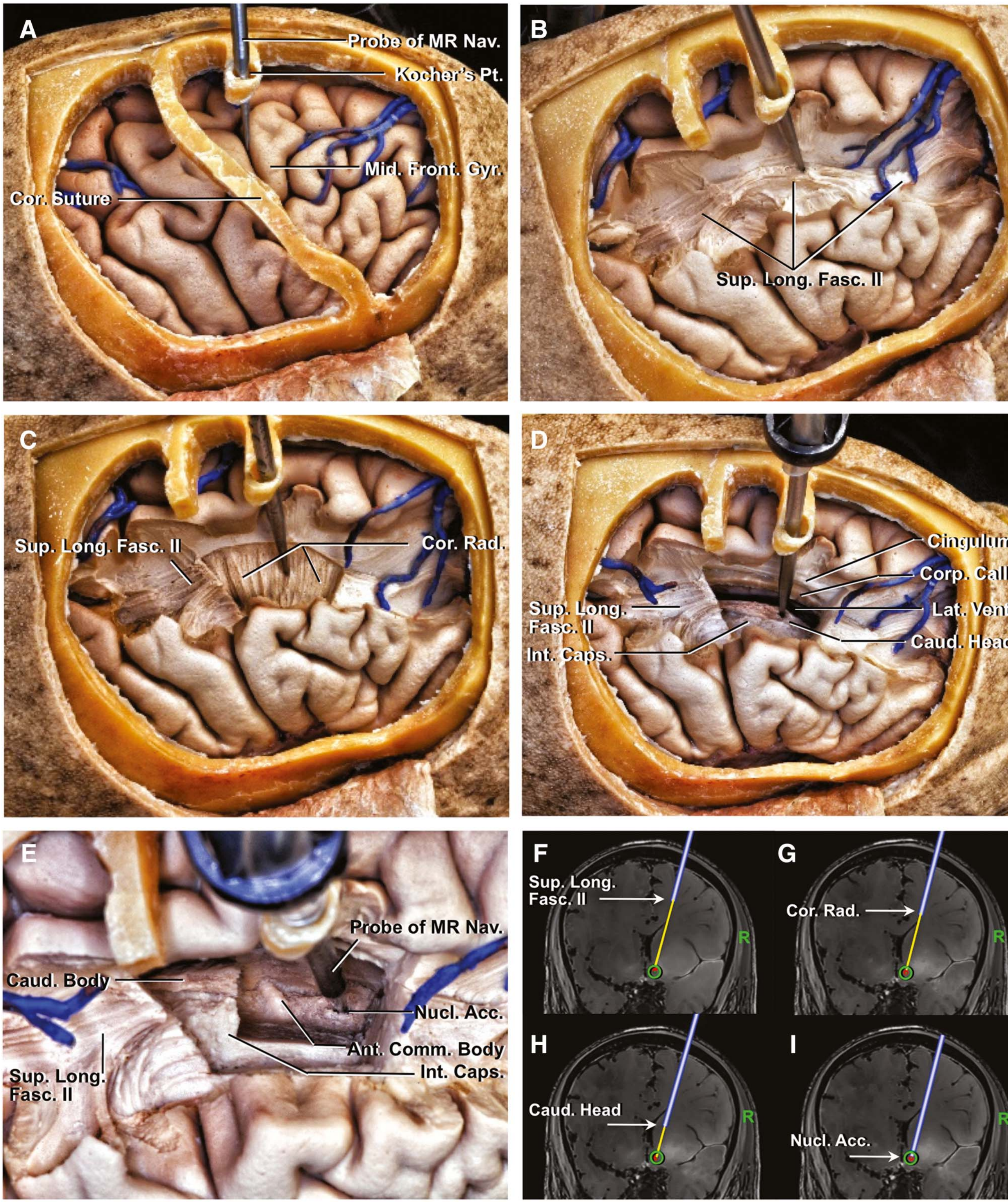

A
Probe of MR Nav.
Kocher's Pt.
Mid. Front. Gyr.
Cor. Suture
B
Sup. Long. Fasc. II
C
Sup. Long. Fasc. II
Cor. Rad.
D
Cingulum
Corp. Call.
Sup. Long. Fasc. II
Lat. Vent.
Caud. Head
Int. Caps.
E
Probe of MR Nav.
Caud. Body
Nucl. Acc.
Ant. Comm. Body
Int. Caps.
Sup. Long. Fasc. II
F
Sup. Long. Fasc. II
R
G
Cor. Rad.
R
H
Caud. Head
R
I
Nucl. Acc.
R

FIGURE 9. *Nucleus accumbens (NAc) exposure with MR navigation.* **A**, *a right frontoparietal craniotomy with preservation of the coronal suture has been performed to show the structures encountered in passing a probe from Kocher's point, 2 cm lateral to the midline and 2 cm anterior to the coronal suture, to the NAc, as used for deep brain stimulation. Opening the dura exposes the middle frontal gyrus.* **B**, *the first tract exposed deep to the U-fibers is the SLF II, underlying the middle frontal gyrus.* **C**, *the anterior part of the SLF II has been reflected posteriorly to expose the corona radiata.* **D**, *removing the corona radiata exposes the head of the caudate nucleus. The lateral ventricle has been exposed medial to the head of the caudate nucleus. The dissection also exposes the corpus callosum and cingulum.* **E**, *the NAc is encountered inferior to the head of the caudate nucleus and anterior to the body of the anterior commissure.* **F-I**, *coronal MR imaging showing the MR navigation in T1-weighted images. The* **arrows** *in* **F-I** *at the junction of the* **blue and yellow trajectories** *show the level at which the superior longitudinal fasciculus II, corona radiata, caudate head, and NAc are encountered in* **B-E**. *The NAc is located at the* **green circle**. *Acc., accumbens; Ant., anterior; Caps., capsule; Caud., caudate; Comm., commissure; Cor., corona; Corp. Call., corpus callosum; Fasc., fasciculus; Front., frontal; Gyr., gyrus; Int., internal; Lat., lateral; Long., longitudinal; Mid., middle; MR, magnetic resonance; Nav., navigation; Nucl., nucleus; Pt., point; Rad., radiata; Sup., superior; Vent., ventricle.*

thalamic peduncle.[24] The anterior thalamic peduncle breaks away from the anterior limb of the internal capsule, and its fibers form a reciprocal connection with the prefrontal and orbitofrontal parts of the cortex and cingulate gyrus.[24]

Some hubs within the limbic loop, especially the NAc, play an important role in psychiatric disorders.[1,9] Targets of DBS providing the greatest clinical benefit in psychiatric disorders have been a subject of debate.[1,9,46] Although many combinations and variations of DBS have been examined in animal models and in human trials, there has been no consensus regarding the anatomic functional features of the best stimulation target in the corticostriatothalamocortical limbic circuit for neuropsychiatric diseases. In 1 study, the stimulation was directed to the NAc.[1] In another study in patients with drug-resistant depression, the limbic loop was stimulated at the subgenual anterior cingulate cortex.[46] As we have shown, the NAc has connections with the subgenual anterior cingulate cortex, orbitofrontal cortex, amygdala, and hypothalamus.[46,72] Rigoard et al[69] pointed out that the accumbofrontal fasciculus, connecting the medial orbitofrontal cortex to the NAc, a part of the corticostriatothalamocortical loop, may be targeted in major depression and OCD. In the same study, the authors also noted that the amygdaloaccumbens

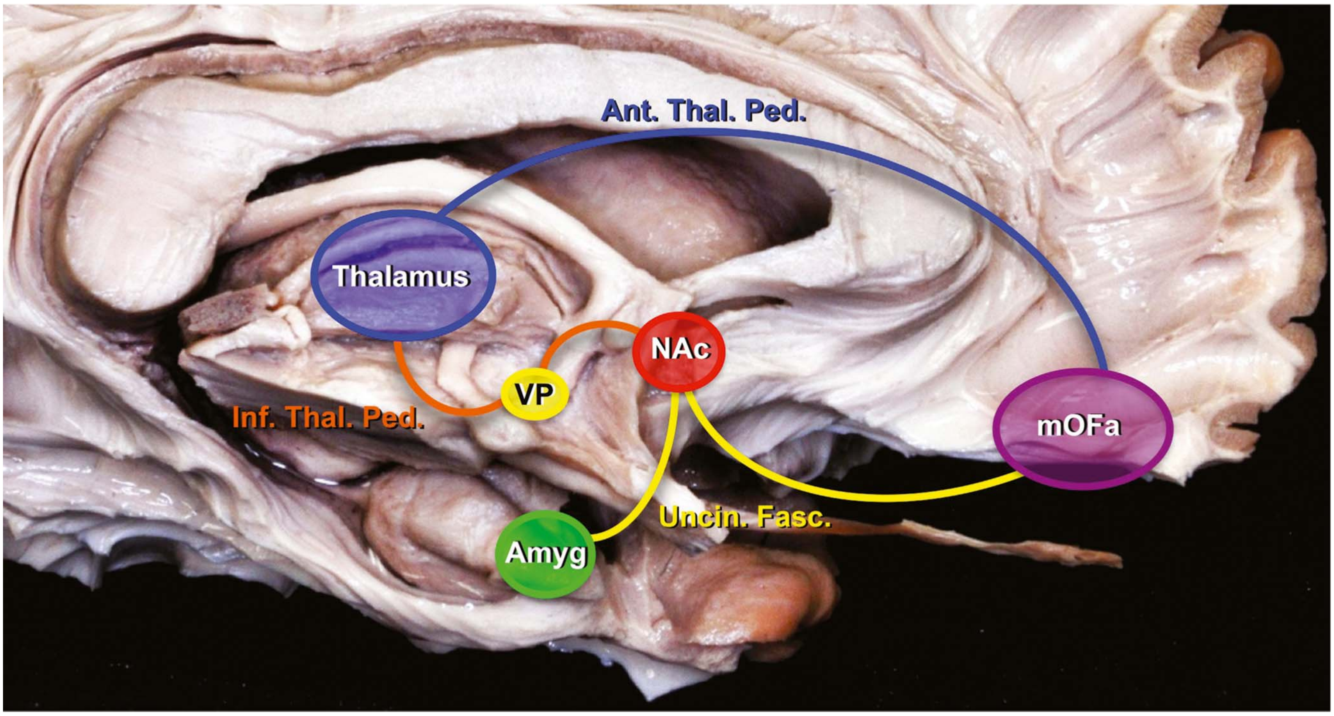


FIGURE 10. *Corticostriatothalamocortical loop. The uncinate fasciculus (***yellow***) conveys information between the medial orbitofrontal area, NAc, and amygdala. The inferior thalamic peduncle (***orange***) connects the NAc to the ventral pallidum and thalamus, and the anterior thalamic peduncle (***blue***) connects the thalamus to the medial orbitofrontal area. Amyg., amygdala; Ant., anterior; Fasc., fasciculus; Inf., inferior; mOFa, medial orbitofrontal area; NAc, nucleus accumbens; Thal. Ped., thalamic peduncle; Uncin., uncinate; VP, ventral pallidum.*

fasciculus connects the amygdala and NAc.[69] In our dissections, the accumbofrontal and amygdaloaccumbens fasciculi appeared to be the ventromedial part of the uncinate fasciculus.

Based on the anatomic relationship of the ventral striatum to limbic areas and to augment the clinical benefits, the dorsal part of the NAc has been targeted with the proximal stimulatory contact extending into the caudate nucleus.[9,46] In another DBS study, the superolateral part of the NAc and adjacent anterior limb of the internal capsule has been targeted.[44] Anterior capsulotomy, division of fibers in the anterior limb of the internal capsule connecting the mediodorsal thalamus reciprocally with the prefrontal cortex as treatment for severe OCD, has previously been completed using stereotactic radiosurgery.[73] Sturm et al[9] have speculated that the beneficial clinical effects of anterior capsulotomy may be the result of blocking the amygdaloid-basal ganglia-prefrontal circuitry at the level of the NAc rather than by directly blocking the internal capsule fibers.

The cingulate pole includes the subcallosal and ventral paracingulate cortices and the posterior part of the prefrontal cortex.[30] The fiber pathways underlying the cingulate pole are the cingulum and uncinate fasciculus and part of the forceps minor. One study reported stimulation of cingulum fibers by DBS placement in the subcallosal cortex.[10] DBS of the cingulate pole may stimulate not only the cingulum, but also the related subcallosal and paracingulate cortices and uncinate fasciculus. On the other hand, the current target for OCD according to Greenberg et al[74] should be at the intersection of the anterior limb of the internal capsule, the anterior commissure, and the posterior ventral striatum, the floor of which is constructed by the ventromedial component of the uncinate fasciculus.

The medial forebrain bundle, which cannot be shown in fiber dissection, connects the ventral tegmental area, dopaminergic center to the septal area, lateral hypothalamus, and frontal cortex in addition to an amygalohypothalamic connection.[24,75] Good outcomes were reported in 6 of 7 patients with drug-resistant depression with stimulation of the medial forebrain bundle, which also activates the limbic corticostriatothalamocortical circuit.[40]

CONCLUSION

An understanding of the connections and cortical and subcortical relationships of the NAc will perhaps enable more accurate DBS targeting for the treatment of psychiatric disorders.

Disclosures

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REFERENCES

1. Bewernick BH, Hurlemann R, Matusch A, et al. Nucleus accumbens deep brain stimulation decreases ratings of depression and anxiety in treatment-resistant depression. *Biol Psychiatry.* 2010;67(2):110-116.
2. de Olmos JS, Heimer L. The concepts of the ventral striatopallidal system and extended amygdala. *Ann N Y Acad Sci.* 1999;877:1-32.
3. Bennett MR. The prefrontal-limbic network in depression: modulation by hypothalamus, basal ganglia and midbrain. *Prog Neurobiol.* 2011;93(4):468-487.
4. Heimer L, Wilson RD. The subcortical projections of the allocortex: similarities in the neural associations of the hippocampus, the piriform cortex, and the neocortex. In: Santini M, ed. *Perspectives in Neurobiology*. New York, NY: Raven Press; 1975: 177-193.
5. Mayberg HS, Lozano AM, Voon V, et al. Deep brain stimulation for treatment-resistant depression. *Neuron.* 2005;45(5):651-660.
6. Zahm DS. Functional-anatomical implications of the nucleus accumbens core and shell subterritories. *Ann N Y Acad Sci.* 1999;877:113-128.
7. Di Chiara G. Nucleus accumbens shell and core dopamine: differential role in behaviour and addiction. *Behav Brain Res.* 2002;137(1-2):75-114.
8. Voges J, Müller U, Bogerts B, Münte T, Heinze HJ. Deep brain stimulation surgery for alcohol addiction. *World Neurosurg.* 2013;80(3-4):S28.e21-e31.
9. Sturm V, Lenartz D, Koulousakis A, et al. The nucleus accumbens: a target for deep brain stimulation in obsessive-compulsive- and anxiety-disorders. *J Chem Neuroanat.* 2003;26(4):293-299.
10. Hamani C, Mayberg H, Snyder B, Giacobbe P, Kennedy S, Lozano AM. Deep brain stimulation of the subcallosal cingulate gyrus for depression: anatomical location of active contacts in clinical responders and a suggested guideline for targeting. *J Neurosurg.* 2009;111(6):1209-1215.
11. Klingler J. Erleichterung der makroskopischen praeparation des gehrins durch den gefrierprozess. *Schweiz Arch Neurol Psychiatr.* 1935;36:247-256.
12. Ludwig E, Klingler J. *Atlas Cerebri Humani*. Basel, Switzerland: S Karger, Inc; 1956:58.
13. Yagmurlu K, Rhoton AL Jr, Tanriover N, Bennett JA. Three-dimensional microsurgical anatomy and the safe entry zones of the brainstem. *Neurosurgery*. 2014;10(suppl 3):602-619.
14. Yagmurlu K, Vlasak AL, Rhoton AL Jr. Three-dimensional topographic fiber tract anatomy of the cerebrum. *Neurosurgery*. 2015;11(suppl 2):274-305.
15. Neto LL, Oliveira E, Correia F, Ferreira AG. The human nucleus accumbens: where is it? A stereotactic, anatomical and magnetic resonance imaging study. *Neuromodulation*. 2008;11(1):13-22.
16. Lucas-Neto L, Neto D, Oliveira E, et al. Three dimensional anatomy of the human nucleus accumbens. *Acta Neurochir (Wien).* 2013;155(12):2389-2398.
17. Salgado S, Kaplitt MG. The nucleus accumbens: a comprehensive review. *Stereotact Funct Neurosurg.* 2015;93(2):75-93.
18. Ongür D, Price JL. The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. *Cereb Cortex.* 2000;10 (3):206-219.
19. Ongür D, Ferry AT, Price JL. Architectonic subdivision of the human orbital and medial prefrontal cortex. *J Comp Neurol.* 2003;460(3):425-449.
20. Hamani C, Mayberg H, Stone S, Laxton A, Haber S, Lozano AM. The subcallosal cingulate gyrus in the context of major depression. *Biol Psychiatry.* 2011;69(4): 301-308.
21. Hendelman W. *Atlas of Functional Neuroanatomy*. 2nd ed. Boca Raton, FL: CRC Press; 2006:230, 234.
22. Powell EW, Leman RB. Connections of the nucleus accumbens. *Brain Res.* 1976; 105(3):389-403.
23. Swanson LW, Cwan WM. A note on the connections and development of the nucleus accumbens. *Brain Res.* 1975;92(2):324-330.
24. Nieuwenhuys R, Voogd J, can Huijzen C. *The Human Central Nervous System*. New York, NY: Springer-Verlag; 2005:247, 253, 291, 293, 341, 363, 414, 596, 917, 921.
25. Heimer L, Harlan RE, Alheid GF, Garcia MM, de Olmos J. Substantia innominata: a notion which impedes clinical-anatomical correlations in neuropsychiatric disorders. *Neuroscience*. 1997;76(4):957-1006.
26. Williams PL, Warwick R. *Gray's Anatomy*. 36th ed. Philadelphia, PA: W.B. Saunders; 1998:995.
27. Tubbs RS, Prekupec M, Loukas M, Hattab EM, Cohen-Gadol AA. The induseum griseum: anatomic study with potential application to callosotomy. *Neurosurgery*. 2013;73(2):312-315.
28. Ebeling U, von Cramon D. Topography of the uncinate fascicle and adjacent temporal fiber tracts. *Acta Neurochir (Wien).* 1992;115(3-4):143-148.
29. Schmahmann JD, Pandya DN. *Fiber Pathways of the Brain*. New York, NY: Oxford University Press; 2006:419, 427, 485.
30. Yaşargil MG. *Microneurosurgery Vol. IV A. Tumors of the Central Nervous System*. Stuttgart, Germany: Georg Thieme; 1994:63.

31. Dejerine J. *Anatomy of the Nervous Centers, Vol. 1 [in French]*. Paris, France: Rueff & Cie; 1895.
32. Fernández-Miranda JC, Rhoton AL Jr, Alvarez-Linera J, Kakizawa Y, Choi C, de Oliveira EP. Three-dimensional microsurgical and tractographic anatomy of the white matter of the human brain. *Neurosurgery*. 2008;62(6 suppl 3):989-1026.
33. Yakovlev PI, Locke S. Limbic nuclei of thalamus and connections of limbic cortex. III. Corticocortical connections of the anterior cingulate gyrus, the cingulum, and the subcallosal bundle in monkey. *Arch Neurol.* 1961;5:364-400.
34. Riva-Posse P, Holtzheimer PE, Garlow SJ, Mayberg HS. Practical considerations in the development and refinement of subcallosal cingulate white matter deep brain stimulation for treatment-resistant depression. *World Neurosurg.* 2013;80(3-4):S27.e25-e34.
35. Lujan JL, Chaturvedi A, Choi KS, et al. Tractography-activation models applied to subcallosal cingulate deep brain stimulation. *Brain Stimul.* 2013;6(5):737-739.
36. Dougherty DD, Rezai AR, Carpenter LL, et al. Randomized sham-controlled trial of deep brain stimulation of the ventral capsule/ventral striatum for chronic treatment-resistant depression. *Biol Psychiatry.* 2015;78(4):240-248.
37. Malone DA Jr, Dougherty DD, Rezai AR, et al. Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. *Biol Psychiatry.* 2009;65(4):267-275.
38. Heilbronner SR, Haber SN. Frontal cortical and subcortical projections provide a basis for segmenting the cingulum bundle: implications for neuroimaging and psychiatric disorders. *J Neurosci.* 2014;34(30):10041-10054.
39. Haber SN, McFarland NR. The concept of the ventral striatum in nonhuman primates. *Ann N Y Acad Sci.* 1999;877:33-48.
40. Schlaepfer TE, Bewernick BH, Kayser S, Mädler B, Coenen VA. Rapid effects of deep brain stimulation for treatment-resistant major depression. *Biol Psychiatry.* 2013;73(12):1204-1212.
41. Carpenter MB. *Core Text of Neuroanatomy*. 4th ed. Baltimore, MD: Williams & Wilkins; 1991:237.
42. Papez JW. A proposed mechanism of emotion. *J Neuropsychiatry Clin Neurosci.* 1995;7(1):103-112.
43. MacLean PD. Psychosomatic disease and the visceral brain; recent developments bearing on the Papez theory of emotion. *Psychosom Med.* 1949;11(6):338-353.
44. Halpern CH, Wolf JA, Bale TL, et al. Deep brain stimulation in the treatment of obesity. *J Neurosurg.* 2008;109(4):625-634.
45. Zahm DS, Brog JS. The significance of subterritories in the "accumbens" part of the rat ventral striatum. *Neuroscience*. 1992;50(4):751-767.
46. Johansen-Berg H, Gutman DA, Behrens TE, et al. Anatomical connectivity of the subgenual cingulate region targeted with deep brain stimulation for treatment-resistant depression. *Cereb Cortex*. 2008;18(6):1374-1383.
47. Smith WK. The results of ablation of the cingular region of the cerebral cortex. *Fed Proc.* 1944;3:42-43.
48. Ward AA Jr. The anterior cingulate gyrus and personality. *Res Publ Assoc Res Nerv Ment Dis.* 1948;27(1 vol):438-445.
49. Sheth SA, Neal J, Tangherlini F, et al. Limbic system surgery for treatmentre-fractory obsessive-compulsive disorder: a prospective long-term follow-up of 64 patients. *J Neurosurg* 2013;118(3):491-497.
50. Patel NV, Agarwal N, Mammis A, Danish SF. Frameless stereotactic magnetic resonance imaging-guided laser interstitial thermal therapy to perform bilateral anterior cingulotomy for intractable pain: feasibility, technical aspects, and initial experience in 3 patients. *Neurosurgery*. 2015;11(suppl 2):17-25.
51. Shields DC, Asaad W, Eskandar EN, et al. Prospective assessment of stereotactic ablative surgery for intractable major depression. *Biol Psychiatry.* 2008;64(6):449-454.
52. Steele JD, Christmas D, Eljamel MS, Matthews K. Anterior cingulotomy for major depression: clinical outcome and relationship to lesion characteristics. *Biol Psychiatry.* 2008;63(7):670-677.
53. Stelten BM, Noblesse LH, Ackermans L, Temel Y, Visser-Vandewalle V. The neurosurgical treatment of addiction. *Neurosurg Focus.* 2008;25(1):E5.
54. Jiménez-Ponce F, Soto-Abraham JE, Ramírez-Tapia Y, Velasco-Campos F, Carrillo-Ruiz JD, Gómez-Zenteno P. Evaluation of bilateral cingulotomy and anterior capsulotomy for the treatment of aggressive behavior. *Cir.* 2011;79(2):107-113.
55. Kim CH, Chang JW, Koo MS, et al. Anterior cingulotomy for refractory obsessive-compulsive disorder. *Acta Psychiatr Scand.* 2003;107(4):283-290.
56. Rhoton AL Jr. The cerebrum. *Neurosurgery*. 2002;51(4 suppl):S1-S51.
57. Yang CR, Mogenson GJ. An electrophysiological study of the neural projections from the hippocampus to the ventral pallidum and the subpallidal areas by way of the nucleus accumbens. *Neuroscience*. 1985;15(4):1015-1024.
58. Airan RD, Meltzer LA, Roy M, Gong Y, Chen H, Deisseroth K. High-speed imaging reveals neurophysiological links to behavior in an animal model of depression. *Science*. 2007;317(5839):819-823.
59. Türe U, Yaşargil MG, Friedman AH, Al-Mefty O. Fiber dissection technique: lateral aspect of the brain. *Neurosurgery*. 2000;47(2):417-426.
60. Kwon HG, Byun WM, Ahn SH, Son SM, Jang SH. The anatomical characteristics of the stria terminalis in the human brain: a diffusion tensor tractography study. *Neurosci Lett.* 2011;500(2):99-102.
61. Avery AS, Clauss JA, Winder DG, Woodward N, Heckers S, Blackford JU. BNST neurocircuitry in humans. *Neuroimage*. 2014;91:311-323.
62. Walker DL, Toufexis DJ, Davis M. Role of the bed nucleus of the stria terminalis versus the amygdala in fear, stress, and anxiety. *Eur J Pharmacol.* 2003;463(1-3):199-216.
63. Anderson VC, Burchiel KJ, Hogarth P, Favre J, Hammerstad JP. Pallidal vs subthalamic nucleus deep brain stimulation in Parkinson disease. *Arch Neurol.* 2005;62(4):554-560.
64. Schlaepfer TE, Cohen MX, Frick C, et al. Deep brain stimulation to reward circuitry alleviates anhedonia in refractory major depression. *Neuropsychopharmacology*. 2008;33(2):368-377.
65. Greenberg BD, Malone DA, Friehs GM, et al. Three-year outcomes in deep brain stimulation for highly resistant obsessive-compulsive disorder. *Neuropsychopharmacology*. 2006;31(11):2384-2393.
66. Bokura H, Robinson RG. Long-term cognitive impairment associated with caudate stroke. *Stroke*. 1997;28(5):970-975.
67. Pellizzaro Venti M, Paciaroni M, Caso V. Caudate infarcts and hemorrhages. *Front Neurol Neurosci.* 2012;30:137-140.
68. Mavridis I, Boviatsis E, Anagnostopoulou S. Anatomy of the human nucleus accumbens: a combined morphometric study. *Surg Radiol Anat.* 2011;33(5):405-414.
69. Rigoard P, Buffenoir K, Jaafari N, et al. The accumbofrontal fasciculus in the human brain: a microsurgical anatomical study. *Neurosurgery*. 2011;68(4):1102-1111.
70. Alheid GF, Heimer L. New perspectives in basal forebrain organization of special relevance for neuropsychiatric disorders: the striatopallidal, amygdaloid, and corticopetal components of substantia innominata. *Neuroscience*. 1988;27(1):1-39.
71. Haber SN, Kunishio K, Mizobuchi M, Lynd-Balta E. The orbital and medial prefrontal circuit through the primate basal ganglia. *J Neurosci.* 1995;15(7 pt 1):4851-4867.
72. Ferry AT, Ongür D, An X, Price JL. Prefrontal cortical projections to the striatum in macaque monkeys: evidence for an organization related to prefrontal networks. *J Comp Neurol.* 2000;425(3):447-470.
73. Lopes AC, Greenberg BD, Canteras MM, et al. Gamma ventral capsulotomy for obsessive-compulsive disorder: a randomized clinical trial. *JAMA Psychiatry.* 2014;71(9):1066-1076.
74. Greenberg BD, Gabriels LA, Malone DA Jr, et al. Deep brain stimulation of the ventral internal capsule/ventral striatum for obsessive-compulsive disorder: worldwide experience. *Mol Psychiatry.* 2010;15(1):64-79.
75. Coenen VA, Panksepp J, Hurwitz TA, Urbach H, Mädler B. Human medial forebrain bundle (MFB) and anterior thalamic radiation (ATR): imaging of two major subcortical pathways and the dynamic balance of opposite affects in understanding depression. *J Neuropsychiatry Clin Neurosci.* 2012;24(2):223-236.

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COMMENT

The nucleus accumbens (NAc) is a central player in regulating responses to our environment. Human imaging studies, as well as animal studies of homologous structures, have helped identify the function and connectivity of this region. In the classic framework of corticobasalthalamocortical loop architecture, the striatum is the major basal ganglia receiving center. The NAc, a major component of the ventral striatum, is the receiving center for much of prefrontal cortex, the most evolutionarily developed region of our brain. It is therefore a critical node in networks regulating reward processing, decision making, and emotional control.

Stereotactic procedures including lesions and deep brain stimulation (DBS) have targeted this region for decades for the treatment of refractory psychiatric conditions, including OCD, depression, addiction, schizophrenia, and others. To a large degree, progress in this field has relied on empirical observations of clinical response to targets of varying location. For example, recent DBS for OCD studies are trying to dissect the contribution of modulating the NAc vs the bed nucleus of the stria terminalis, a gray matter region just posterior to the NAc. The precise connectivity and function of these regions is still incompletely understood.

In this study, the authors use standard cadaveric dissection techniques to study the microsurgical white matter anatomy of the NAc region. They identify a number of tracts connecting the NAc to medial and orbital prefrontal cortex, the mesial temporal lobe, and the septal region. Appreciation of the microanatomy and connectivity of the NAc with this level of granular detail will improve our ability to develop neuromodulatory treatments for psychiatric and behavioral disorders.

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