



# Three-Dimensional Dissection of the Bed Nucleus of the Stria Terminalis and Its White Matter Connections: A Surgical and Neuropsychiatric Perspective

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## ABSTRACT

**AIM:** To provide an in-depth anatomical description of the bed nucleus of the stria terminalis (BST) and its structural affiliations, with an emphasis on its surgical and neuromodulatory relevance.

**MATERIAL and METHODS:** We conducted stepwise fiber dissections on 14 formalin-fixed human brains prepared using the Klingler method. Under high magnification, dissections were performed lateral to medial and medial to lateral directions, enabling detailed visualization of the BST's relationship with adjacent fiber tracts and nuclei such as the anterior commissure, fornix, stria terminalis, nucleus accumbens, and septal area.

**RESULTS:** The BST was consistently located anterosuperior to the anterior commissure and medially bordered by the septal nuclei, forming a compact yet integrative structure. Dense projections were identified between the BST and limbic-hypothalamic targets via the stria terminalis, fornical fibers, and the diagonal band of Broca. These connections emphasize the BST's pivotal position in coordinating limbic output with neurovegetative centers.

**CONCLUSION:** This study refines the topographic and connectional map of the BST, offering structural insight into its role as a limbic hub. Such clarity may assist in tailoring neuromodulatory interventions—such as deep brain stimulation—by improving anatomical precision in disorders involving fear, compulsion, and affect regulation.

**KEYWORDS:** Bed nucleus of the stria terminalis, White matter, Fiber dissection, Limbic system, Deep brain stimulation

**ABBREVIATIONS:** **AC:** Anterior commissure, **BST:** Bed nucleus of the stria terminalis, **CdN:** Caudate nucleus, **DBB:** Diagonal band of Broca, **NAC:** Nucleus accumbens; **OCD:** Obsessive-compulsive disorder, **SI:** Substantia innominata, **ST:** Stria terminalis, **VAFP:** Ventral amygdalofugal pathway

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## ■ INTRODUCTION

The bed nucleus of the stria terminalis (BST) is a compact yet anatomically and functionally complex cluster of neuronal nuclei located within the basal forebrain, maintaining close structural and functional associations with the limbic system (12,27). These nuclei are conventionally divided into a narrow dorsolateral segment positioned dorsally to the amygdaloid complex, an intermediate zone extending along the stria terminalis (ST), and a ventromedial expansion situated near the crossing fibers of the anterior commissure (AC) (26,27). Anatomically, the BST forms extensive connections with structures such as the fornix, ST, AC, nucleus accumbens (NAc), and septal nuclei. These connections facilitate neuroanatomical integration with major limbic components including the hippocampus, amygdala, hypothalamus, and prefrontal cortex (2,8,27).

Experimental and clinical studies have consistently demonstrated the pivotal role of the BST in stress response, anxiety-related processes, social behaviors, and sustained emotional regulation (19,32,33). Moreover, in progressive neurodegenerative conditions such as Alzheimer's disease, it has been proposed that disruptions in the BST's connectivity with key limbic pathways—such as the ST and fornix—may contribute to the deterioration of cognitive and emotional functions (11,28). Consequently, the BST has emerged as a neuromodulatory target in a variety of neuropsychiatric conditions, including obsessive-compulsive disorder (OCD), major depressive disorder, anorexia nervosa, and Alzheimer's disease (4,9,10,21-23,25,36).

The BST is surrounded by dense white matter pathways, and the complexity of its internal organization has recently garnered increased attention through cadaveric dissections and advanced neuroimaging techniques (1,19,31). However, the limited volume of this region and the indistinct boundaries with neighboring gray matter structures pose challenges for achieving precise anatomical resolution using noninvasive methods (31).

The present study, aimed to systematically investigate the white matter connectivity of the BST in the human brain through cadaveric dissection, and to evaluate the clinical implications of the findings in light of current literature. These anatomical insights are anticipated to support the refinement of BST-targeted interventions, particularly in the context of neuropsychiatric disorders.

## ■ MATERIAL and METHODS

### Cadaveric Dissection

This study designed to investigate the three-dimensional anatomical organization of the BST and its surrounding white matter pathways, was based on cadaveric dissection techniques. Fourteen postmortem human brain specimens prepared according to the Klingler method were utilized (15). The specimens were fixed in 10% formaldehit solution for a minimum of eight weeks, then frozen at  $-16^{\circ}\text{C}$  for two weeks to facilitate fiber dissection. After thawing in running

water, stepwise layer by layer dissections were performed from lateral to medial and medial to lateral directions. All dissections were carried out under a stereomicroscope, and the white matter pathways were meticulously exposed with preservation of anatomical integrity. Special emphasis was placed on identifying the AC, fornix, ST, and septal areas surrounding the BST, and each stage of the dissection was documented with high-resolution three-dimensional imaging in accordance with the protocol described by Shimizu et al. (30).

### Ethical Considerations

Since the cadavers were used solely for educational and scientific observational purposes, no additional institutional review board approval was required.

## ■ RESULTS

### Lateral to Medial Dissection

The dissection process was initiated at the central core of the insula and advanced systematically in a lateral to medial direction. In this sequence, the external capsule, putamen, globus pallidus, internal capsule, thalamic peduncles, thalamus, and caudate nucleus (CdN) were identified from superficial to deep layers (Figure 1A). Upon removal of the putamen and globus pallidus, the posterior limb of the AC projecting posterolaterally and the anterior limb extending anterolaterally were clearly distinguished beneath these structures (Figure 1A). The substantia innominata (SI), including the anterior perforated substance, was identified in the region between the anterior commissural fibers and the uncinate fasciculus. The anteromedial boundary of this region was defined by the anterior limb of the AC, the posterolateral boundary by its posterior limb, and the lateral boundary by the uncinate fasciculus (Figure 1A).

Following the removal of the internal capsule fibers, the thalamus located at the medial core and the CdN arching around it in a C-shaped configuration became clearly visible. The inferolateral segment of the ST originated from the amygdala, coursed medial to the CdN, and traversed posteriorly beneath Meyer's loop. Ascending along the striothalamic sulcus, ST encircled the thalamus dorsally and turned anteriorly along its superior border. As it turned inferiorly in the anterior thalamic region, it terminated on the posterolateral surface of the BST, in close anatomical relation to the NAc and the AC (Figure 1C, 1D).

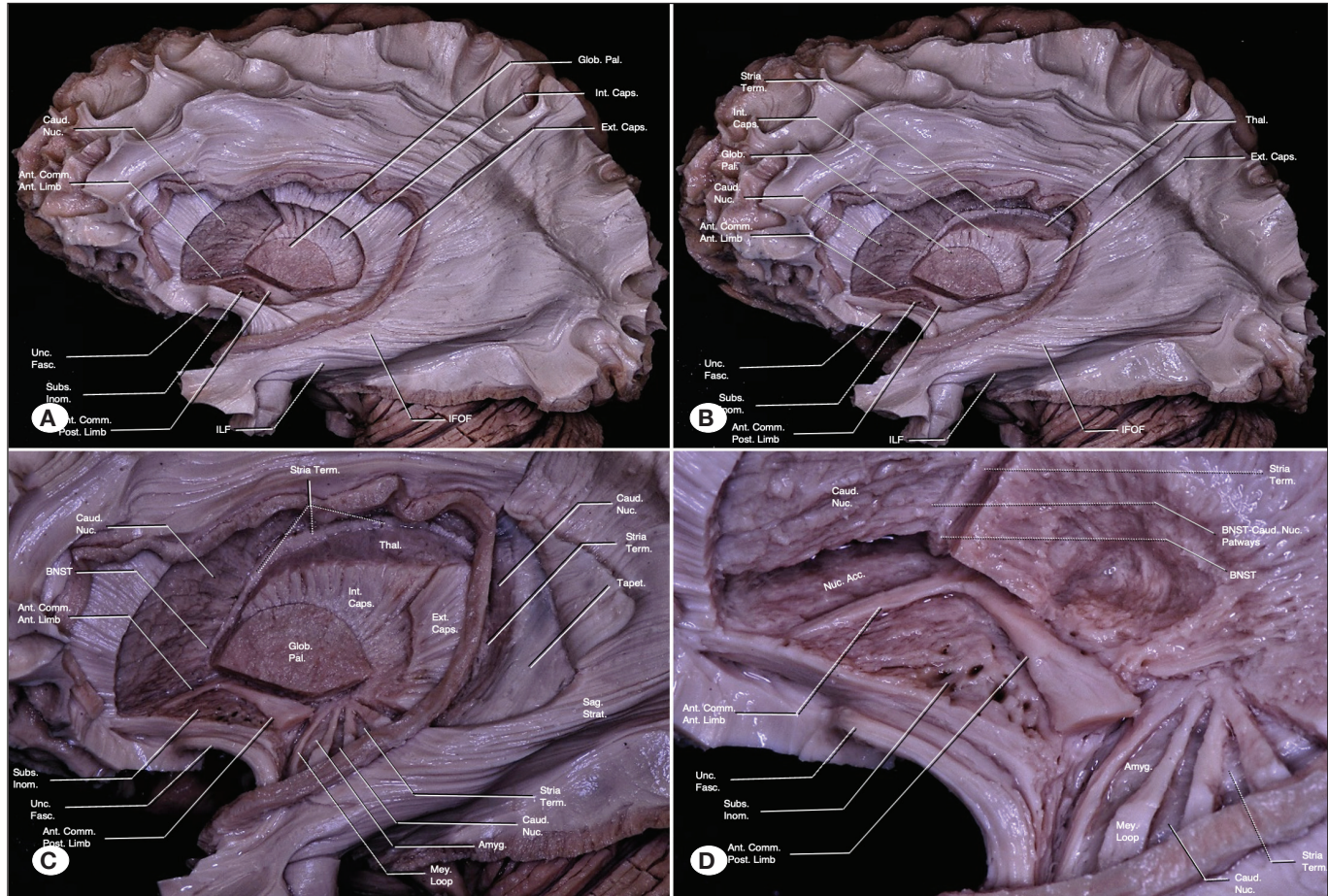
In lateral to medial dissections, the BST was identified anterosuperior to the AC, posterosuperior to the NAc, anteromedial to the thalamus, and posteroinferior to the CdN (Figure 1D).

### Medial to Lateral Dissection

Prior to initiating the medial to lateral dissection, the corpus callosum and cingulum fibers were removed. This step clearly revealed the CdN along the lateral wall of the lateral ventricle, forming a C-shaped arc surrounding the thalamus (Figure 2A). The crus of the fornix extended anteriorly to the level of the AC, situated adjacent to the head of the CdN and the anterior border of the thalamus—an area overlapping with the BST

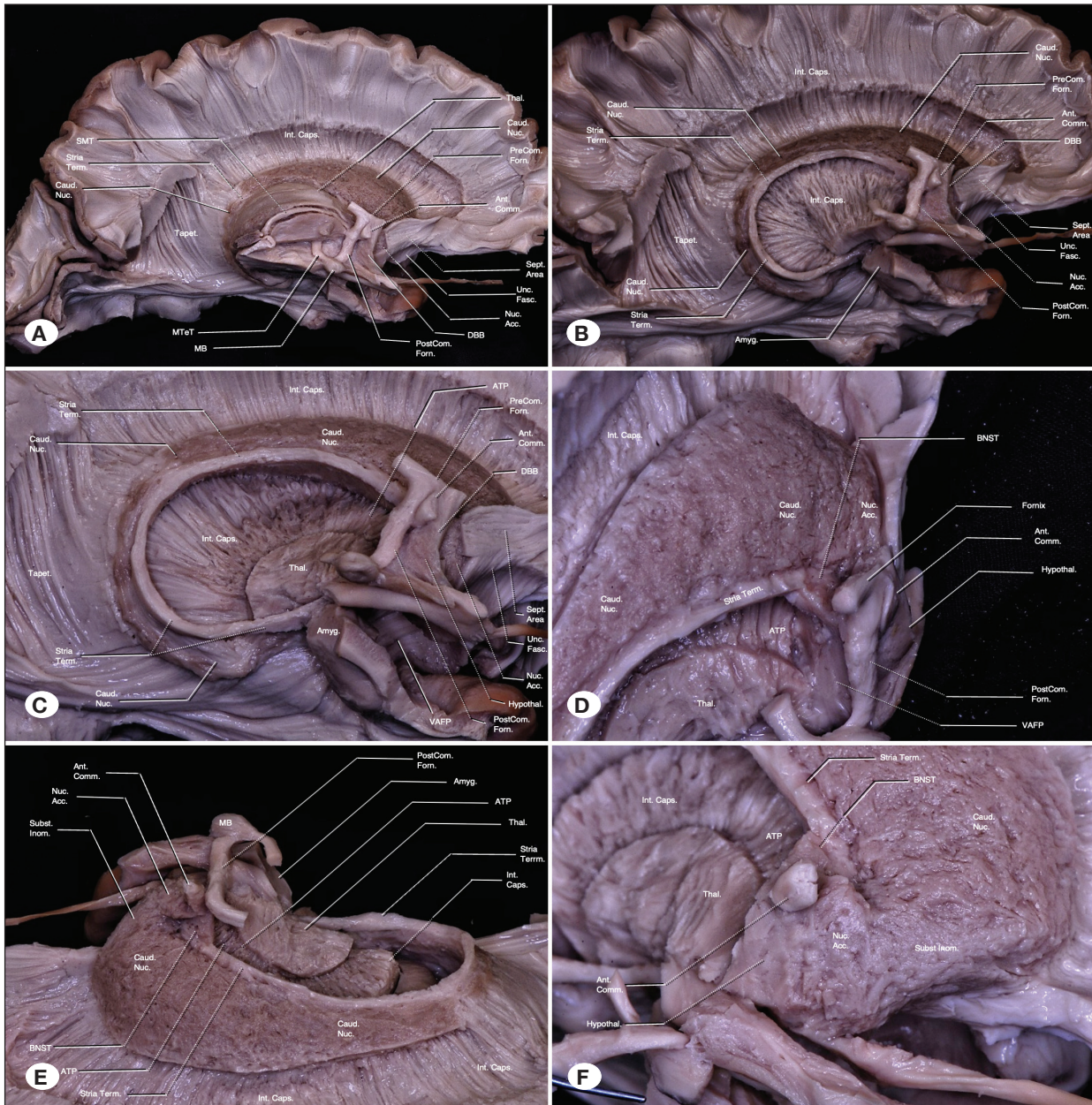
(Figure 2B, 2C, 2D). Just above the AC, the fornix divided into two branches: the postcommissural fornix, descending posteroinferiorly along the posterior hypothalamus toward the mammillary bodies, and the precommissural fornix, projecting anteroinferiorly to approach the rostral portion of the BST medially, in close association with the diagonal band of Broca (DBB) and the septal area (Figure 2B, 2C, 2D).

Positioned superior to the posterior commissure and adjacent to the dorsal aspect of the pineal gland, the habenular commissure gives rise to the stria medullaris thalami, which courses along the medial surface of the thalamus within the lateral wall of the third ventricle. The stria medullaris thalami receives projections from the preoptic and hypothalamic regions as well as the septal area, and it travels anteriorly along the mediobasal thalamus, passing close to the inferior margin of the BST (Figure 2A).



**Figure 1:** Demonstration of the anatomical relationships of the BNST through lateral to medial dissection. **A)** A central core dissection was performed from the lateral aspect of the brain. Removal of the putamen reveals the underlying globus pallidus and internal capsule fibers. At the base of the putamen lie the substantia innominata and the anterior commissure. When the anterior limb of the internal capsule and the anterior thalamic peduncle fibers are removed, the head of the caudate nucleus becomes visible. **B)** Deep to the internal capsule and the superior thalamic peduncle fibers lie the thalamus and the superior extension of the caudate nucleus. The stria terminalis courses along the striatal-thalamic sulcus located between the thalamus and the caudate nucleus. **C)** Removal of the posterior limb of the internal capsule reveals the tail of the caudate nucleus and the medially positioned stria terminalis. By creating windows among the fibers forming Meyer's loop, the anatomical relationship among the amygdala, the caudate nucleus tail, and the stria terminalis was demonstrated. **D)** Closer view. The stria terminalis, originating from the amygdala, traverses medially to the caudate nucleus, proceeds posteriorly, ascends dorsally beneath Meyer's loop, and curves anteriorly following the superior margin of the thalamus. Upon reaching the anterior thalamic region, it turns inferiorly to reach the posterolateral surface of the BST. This segment of the stria terminalis is in close proximity to the nucleus accumbens and the anterior commissure. The BST was anatomically localized anterosuperior to the anterior commissure, posterosuperior to the nucleus accumbens, posteroinferior to the caudate nucleus, and anteromedial to the thalamus. **Amyg.:** amygdala; **Ant. Comm. Ant. Limb:** anterior limb of the anterior commissure; **Ant. Comm. Post. Limb:** posterior limb of the anterior commissure; **BNST:** bed nucleus of the stria terminalis; **Caud. Nuc.:** caudate nucleus; **Ext. Caps.:** external capsule; **Glob. Pal.:** globus pallidus; **IFOF:** inferior fronto-occipital fasciculus; **ILF:** inferior longitudinal fasciculus; **Int. Caps.:** internal capsule; **Mey. Loop:** Meyer's Loop; **Nuc. Acc.:** nucleus accumbens; **Sag. Strat.:** sagittal stratum; **Stria Term.:** stria terminalis; **Subs. Inom.:** substantia innominata; **Tapet.:** tapetum; **Thal.:** thalamus; **Unc. Fasc.:** uncinat fasciculus.





**Figure 2:** Demonstration of the anatomical relationships of the BNST through medial to lateral dissection. **A)** After removal of the corpus callosum and cingulum fibers, the caudate nucleus extending along the medial wall of the lateral ventricle becomes visible. The caudate nucleus exhibits a C-shaped configuration encircling the thalamus. The stria medullaris thalami, arising from the habenular commissure, courses anteriorly along the dorsomedial surface of the thalamus toward the hypothalamic area. The crus of the fornix projects toward the anterior commissure and is adjacent to both the head of the caudate nucleus and the anterior thalamic nuclei. At this level, the fornix is located in a plane overlapping the BNST. **B)** Following removal of the thalamus, fibers of the internal capsule were exposed. **C)** Closer view. The thalamus is partially removed, with the anterior thalamic peduncle preserved; elsewhere, the internal capsule is revealed. The anterior thalamic peduncle obliquely traverses the BNST from the lateral side. Just above the anterior commissure, the fornix splits into precommissural and postcommissural components. The precommissural fibers of the fornix cross the medial surface of the BNST in close relation to the diagonal band of Broca. The C-shaped course of the stria terminalis, along with the caudate nucleus, originating from the amygdala, was observed. **D-F)** Oblique posteromedial (**D**), superomedial (**E**), and anteromedial (**F**) views depict the anatomical relationships of the BNST. The nucleus accumbens, substantia innominata, and the caudate nucleus were observed to encircle the BNST from the anterior aspect. **Amyg.:** amygdala; **Ant. Comm.:** anterior commissure; **ATP:** anterior thalamic peduncle; **BNST:** bed nucleus of the stria terminalis; **Caud. Nuc.:** caudate nucleus; **DBB:** diagonal band of Broca; **Hypothal.:** hypothalamus; **Int. Caps:** internal capsule; **MB:** mammillary body; **MTet:** mamilloreticular tract; **Nuc. Acc.:** nucleus accumbens; **PostCom. Forn.:** postcommissural fornix; **PreCom. Forn.:** precommissural fornix; **Sept. Area:** septal area; **SMT:** stria medullaris thalami; **Stria Term.:** stria terminalis; **Subst. Inom.:** substantia innominata; **Tapet.:** tapetum; **Thal.:** thalamus; **Unc. Fasc.:** uncinatus fasciculus; **VAEP:** ventral amygdalofugal pathway.

Upon removal of the thalamus and lateral mesencephalon, the medial surface of the temporal lobe was exposed, revealing the amygdala (Figure 2B). Fibers originating from the amygdala formed the dorsal amygdalofugal pathway, which coursed inferomedially around the CdN and followed the striothalamic sulcus as the ST. This bundle curved dorsally over the thalamus and terminated in the BST, situated at the anterosuperior aspect of the AC. Before reaching the BST, the ST passed medially between the postcommissural fornix and the anterior thalamic peduncle. As it passed superior to the AC, it reached the BST in association with the precommissural fornix, the DBB, and the anterior hypothalamic area (Figure 2C, 2D, 2E, 2F).

The anterior portion of the BST was bordered by the head of the CdN and the NAc. Fibrous continuity was observed between the posterosuperomedial portion of the NAc and the BST. Anteroinferiorly, the BST was in close anatomical relation with the SI.

#### **Anatomical Neighborhood and Fiber Connections of the Bed Nucleus of the Stria Terminalis**

Dissections revealed that the BST is located on the anterolateral wall of the third ventricle and is in direct anatomical continuity with several neighboring structures, including the AC, NAc, CdN, SI, septal area, and gyrus paraterminalis (Table I). The AC was observed along the dorsal border of the BST, while the NAc was situated anteroinferiorly and the SI anteroinferiorly and laterally. The septal area was located medially to the BST, and the gyrus paraterminalis occupied a rostral position.

Examination of fiber pathways demonstrated that projections to the BST course through the ST, pre- and postcommissural fornix, AC, DBB, and stria medullaris thalami (Table II). Fibers of the ST, originating from the amygdala, formed a posterior, superior, and anterior arch before reaching the posterolateral surface of the BST. Precommissural fornix fibers approached the rostral BST medially, whereas postcommissural fornix fibers coursed medially to the caudal BST and continued

toward hypothalamic structures. Fibers of the DBB were observed along the inferomedial border of the BST, and the posterior limb of the AC passed adjacent to its dorsal margin.

#### **DISCUSSION**

This study aimed to revisit the anatomical localization and white matter connectivity of the BST in the human brain through detailed cadaveric dissections, thereby elucidating its position within the broader limbic network. The findings demonstrated that the BST is structurally interconnected with adjacent regions such as the AC, NAc, CdN, and thalamus (Table I, Figures 1-2), and that its afferent and efferent pathways—most notably the fornix, ST, and ventral amygdalofugal pathway (VAFP)—position the BST not as an isolated structure, but rather as a central node within a highly integrated connectational system. This comprehensive network architecture suggests that the BST is not merely a relay station, but an active modulator in processes such as emotional regulation, stress response, and autonomic control (1,7,8,19,33).

The connectivity pattern of the BST exhibits a bidirectional organizational model through both long-range projections (along the anteroposterior axis) and short-range local projections (Table II). Through major pathways such as the ST, VAFP, and the fornix, the BST maintains structural continuity with key limbic centers including the hippocampus, amygdala, and hypothalamus, thus actively participating in emotional information processing, stress regulation, and memory-related functions. In contrast, its short-range projections with structures such as the NAc, septal complex, and SI suggest a modulatory role in region-specific autonomic and affective responses (5,6,8,13,14,18-20,31).

Our dissections revealed that the ST approaches the BST from a posterolateral trajectory to establish connections with the amygdaloid complex (Figures 1C, 1D, 2B, 2C), supporting its role in the transmission of emotional information (5,8). In this context, the C-shaped course of the ST between the thal-

**Table I:** Anatomical Neighborhood of the Bed Nucleus of the Stria Terminalis

Structure	Anatomical Relationship with the BST
Anterior Commissure	Located anterosuperior to the BST; closely associated with its dorsal border.
Nucleus Accumbens	Positioned anteroinferior to the BST; maintains short-range reciprocal connections.
Caudate Nucleus (Head)	Situated anterolateral to the BST; together with the NAc, forms the anterior border.
Anterior Thalamic Peduncle	Extends anterosuperiorly from the posterolateral aspect of the BST.
Substantia Innominata	Located anteroinferior to the BST; provides short fiber connections and receives projections via the VAFP.
Third Ventricle	The BST is located on the anterolateral wall of the third ventricle..
Fornix	Passes posterior and medial to the BST.
Gyrus Paraterminalis	Forms the rostral anterior neighborhood of the BST.
Hypothalamic Region	Situated caudally to the BST.
Septal Area	Located medially to the BST; establish dense structural connections.



**Table II:** Fiber Connections of the Bed Nucleus of the Stria Terminalis

Fiber	Source	Course	Relation to the BST
Stria Terminalis	Amygdala	Arches posteriorly, superiorly, anteriorly, and inferiorly around the CdN	Terminates at the posterolateral surface of the BST; conveys strong amygdaloid projections
Precommissural Fornix	Hippocampus	Passes anterior to the AC in an anteroinferior direction	Reaches the rostral BST medially; structurally interacts with the DBB and septal areas
Postcommissural Fornix	Hippocampus	Projects inferoposteriorly after passing posterior to the AC	Approaches the caudal BST medially; continues toward the posterior hypothalamus and mammillary bodies
Anterior Commissure	Contralateral hemisphere	Fibers pass near the posteroinferior margin of the BST via the posterior limb	Lies adjacent to the dorsal border of the BST; some BST fibers may cross hemispheres via this structure
Stria Medullaris Thalami	Habenular commissure	Courses anteriorly along the mediobasal thalamus	Passes near the inferior margin of the BST; provides projections to septal and hypothalamic areas
Diagonal Band of Broca	Fibers diverging from the VAFP	Ascends superomedially beneath the AC	Closely related to the medial and inferior borders of the BST
Hypothalamic Projections	Originating from the BST	Extend caudally and inferiorly	Project to the preoptic region and anterior hypothalamus; form caudal efferent connections of the BST

amus and CdN has been previously documented in the literature, and our anatomical findings align structurally with these descriptions (Figure 2A, 2B, 2C) (8,14,18,20,35). Furthermore, the points of contact with the DBB suggest that the BST maintains bidirectional communication with the amygdala via the VAFP.

Our dissection data also demonstrated that the BST establishes particularly robust structural relationships with the septal areas, predominantly in its medial and ventral aspects (Figure 2A, 2B, 2C). The division of the fornix into precommissural and postcommissural branches, each approaching the BST from dorsal and medial directions, respectively, indicates that this nucleus maintains bidirectional connectivity with both anterior limbic structures (such as the septal region and prefrontal cortex) and posterior components (including the hypothalamus and mammillary bodies). Notably, the observation that precommissural fornix fibers reach the dorsal portion of the BST and proceed toward the medial septal and hypothalamic regions supports the notion that the BST serves as a critical transitional station between cortical and limbic systems (Figure 2C, 2D).

The close anatomical relationship between the AC and the BST was clearly observed in our dissections and may indicate a potential role for these structures in interhemispheric regulation of emotional processes (Figure 1C, 1D) (1,27). In their detailed fiber dissection of the septum verum, Barany et al. also demonstrated that projections passing around the AC facilitate information transfer between the BST and septal

areas (1). These findings suggest that the BST is not only a component of the limbic system but may also function as a dynamic interface governing bidirectional information flow between cortical and subcortical regions.

Our dissection findings also revealed a distinct anatomical relationship between the BST and the SI in the anteroinferior plane (Figures 1D, 2F). This close spatial association may serve as a structural bridge between the BST and subcortical centers involved in arousal, attention, and visceral regulation within the basal forebrain (27,32). Accordingly, the BST can be considered not only as a conduit for afferent–efferent information transfer but also as a functionally active structure contributing to the maintenance of emotional stability.

Consistent with current literature, our study demonstrated that the stria medullaris thalami courses along the inferior margin of the BST, projecting to septal and hypothalamic regions (Figure 2A) (1,16,29). This anatomical connection may represent a component of an integrated system supporting the neural basis of emotional signal processing, impulse regulation, and autonomic coordination among the dorsal thalamus, habenular complex, and hypothalamus (27,29).

The BST has recently emerged as a key target in deep brain stimulation (DBS) research, particularly in treatment-resistant OCD (4,24,25). In their study involving 11 patients, Naesström et al. reported that DBS targeting the BST generated an electrical field extending beyond the nucleus itself to adjacent structures such as the internal capsule, AC, fornix, and globus pallidus—resulting in clinically significant improvements (25).

The anatomical proximity and connectivity of the BST suggest that it functions as a bidirectional regulatory hub capable of modulating affective and compulsive symptom domains (4,24,25). Its spatial relationship with the AC and NAc further supports its potential role in emotional decision-making and impulsivity regulation via the ventral striatal circuitry (25,34). Based on these observations, our dissection results closely align with the proposed therapeutic targets, reinforcing the functional significance of the BST as a viable intervention site in the treatment of OCD.

Considering the BST as a surgical target highlights the critical importance of anatomical precision in neuromodulation techniques such as DBS. Our findings support the view that even millimeter deviations in electrode placement relative to surrounding structures such as the AC, internal capsule, NAc, SI, fornix, and globus pallidus may significantly influence clinical outcomes, based on the anatomical data obtained in this study (22,24,25). Accordingly, comprehensive mapping of the BST and its neighboring structures is essential not only for accurate targeting but also for maximizing therapeutic efficacy.

The pivotal role of the BST in emotional regulation has led to its consideration as an alternative DBS target not only in OCD but also in treatment-resistant depression and generalized anxiety disorder (3,10,34). Several long-term studies have reported that bilateral DBS targeting the BST yields clinically meaningful improvements in both anxiety and depressive symptoms (3,10,23,34). These findings underscore the BST's importance as a neuromodulatory center interacting not only with the limbic system, but also with regulatory components such as the prefrontal cortex, medial septal region, and hypothalamus (3,7,17,19). The medial approach of the fornix fibers identified in our dissections, as well as the connections with the underlying SI and the anteroinferiorly situated DBB, support the BST's integrative role within the hypothalamo-septal and cortico-limbic networks.

### Limitations

Despite the significance of the findings, this study carries several methodological limitations. The use of postmortem human brain specimens restricted the analysis to anatomical connections only, precluding the direct observation of physiological functions or dynamic interactions. Additionally, technical challenges encountered during the dissection of fine fiber bundles may have led to the omission or underrepresentation of certain connections. However, these limitations were mitigated as much as possible by conducting meticulous dissections and continuously validating the findings against existing literature.

### CONCLUSION

Our study contributes to both neuroscience and neuromodulation by thoroughly delineating the fiber connectivity of the BST and its anatomical relationships with surrounding structures. By identifying its connections with the AC, fornix, ST, NAc, SI, thalamus, hypothalamus, and amygdala, the present findings

support previous studies concerning the role of the BST in emotional regulation, stress response, and the pathophysiology of affective disorders. We consider that these anatomical results provide a significant basis for improving the accuracy of surgical targeting in neuromodulatory interventions. Furthermore, these findings suggest that the BST should be considered a key target in the neuromodulation-based treatment of clinical conditions such as depression, OCD, and generalized anxiety disorder.

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### Declarations

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**Availability of data and materials:** The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

**Disclosure:** The authors declare no competing interests.

### AUTHORSHIP CONTRIBUTION

Study conception and design: OB, SSB, NT

Data collection: OB, OMC, SSB

Analysis and interpretation of results: OB, YED

Draft manuscript preparation: OB, YED, OMC, SSB

Critical revision of the article: OB, SSB, CC, NT

Other (study supervision, fundings, materials, etc.): NT

All authors (OB, YED, OMC, SSB, CC, NT) reviewed the results and approved the final version of the manuscript.

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