Anatomy of the subthalamic nucleus, with correlation of deep brain stimulation

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OBJECT The goal in this study was to examine the cadaveric anatomy of the subthalamic nucleus (STN) and to analyze the implications of the findings for deep brain stimulation (DBS) surgery.

METHODS Five formalin-fixed human cerebroms were dissected using the Klingler fiber dissection technique. Digital photographs of the dissections were fused to obtain an anaglyphic image.

RESULTS The STN was located posteroinferior to the anterior corticospinal fibers, posterosuperior to the substantia nigra, and anteromedial to the red nucleus, lenticular fasciculus, and thalamic fasciculus. The subthalamic region is ventral to the thalamus, medial to the internal capsule, and lateral and caudal to the hypothalamus. The nuclei found within the subthalamic region include the STN. The relationship between the STN and surrounding structures, which are not delineated sharply, is described.

CONCLUSIONS The fiber dissection technique supports the presence of the subthalamic region as an integrative network in humans and offers the potential to aid in understanding the impacts of DBS surgery of the STN in patients with Parkinson disease. Further research is needed to define the exact role of the STN in the integrative process.

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The subthalamic nucleus (STN) is an important part of the brain related to Parkinson disease (PD) and other involuntary movements. The STN contains some fibers that travel to the cortical area and basal ganglia.2 The STN is located just superomedial to the red nucleus and substantia nigra. Widely acknowledged as an important modulator of basal ganglia output, the STN receives its major afferents from the cerebral cortex, thalamus, globus pallidus externus (GPe), and brainstem. The STN projects mainly to both segments of the GP, substantia nigra, striatum, and brainstem and is essentially composed of glutamatergic neurons. Lesions of the STN induce choreiform abnormal movements and ballism on the contralateral side of the body.2,3 Despite current interest, little is known about the relation between function of the STN and movement. In this study we describe the anatomical relationship between the STN and surrounding structures.

Methods

Anatomical Study

The cerebral hemispheres and cerebroms of 5 human cadavers were fixed in a 10% formalin solution for at least 3 weeks. The first step in the preparation of the specimens was the removal of the arachnoidal and vascular structures with the aid of a surgical microscope (magnification range ×6 to ×40). The hemispheres were frozen at −16°C for 2–4 weeks. Twenty-four hours after completion of the freezing process, the white fiber dissection was done with fine and...
self-shaped wooden spatulas. We took numerous digital photographs during dissections and, using a specific software program (Anamaker 3D; available free from www.stereoeye.com), we fused the images to obtain an anaglyphic image.

**Results**

**Anatomical Dissection**

The dissection of the brain is started from the gray matter of the cortex, and U-fibers are observed under the gray matter. After the removal of U-fibers, the cortical fibers are seen. To expose the superior longitudinal fasciculus, we remove the cortical gray matter; adjacent superficial short fibers of the frontal, temporal, and parietal opercula; the middle, frontal, superior, and middle temporal gyri; and the inferior parietal lobe. The first identified fasciculus in dissection, which begins on the lateral hemispheric surface, is the superior longitudinal (arcuate) fasciculus. Traditionally, this fasciculus can be described as a reversed C-shaped structure, which surrounds the insula and interconnects the frontal and temporal lobes (Fig. 1).

At a deeper level in the temporo-parietal area, a group of fibers arching around the posterosuperior insular border is seen to be traveling between the posterior temporal region and the prefrontal area. These fibers form the frontotemporal or arcuate segment of the superior longitudinal fasciculus. By dissecting the inferolateral hemispheric surface, we can see a group of fibers deep to the temporo-parietal segment of the superior longitudinal fasciculus (Fig. 1).

Progressive dissection of the fibers of the superior longitudinal fasciculus reveals the insular cortex. After removal of the insular subcortex, we can see the white fibers of the extreme capsule; and at the level of the limen insula, the fibers of the uncinate and inferior occipitofrontal fascicles can be distinguished. The extreme capsule is a group of fibers situated between the insular cortex and the claustrum (Fig. 1).

The external capsule is composed of fibers situated between the claustrum and the putamen. By removing the fibers of the dorsal extreme capsule, we can see the fibers of the dorsal external capsule at the periphery of the dorsal claustrum. At the level of the limen insula, the uncinate fasciculus and inferior frontooccipital fasciculus can be observed (Fig. 1).

After dissection of the crus cerebri, we first observe the substantia nigra, which is located superolateral to the red nucleus. When the red nucleus is dissected, fibers of the ansa lenticularis can be observed. The STN is located postero-inferior to the anterior corticospinal fibers, posterosuperior to the substantia nigra, and anteromedial to the red nucleus, lenticular fasciculus, and thalamic fasciculus. The STN had a café-au-lait color in cadaver sections (Fig. 2).

**Identification of the STN**

The STN is a small, lens-shaped nucleus in the brain. The STN is a part of the basal ganglia system and is located ventral to the thalamus, dorsal to the substantia nigra, and medial to the internal capsule (Fig. 3). Anterior and lateral borders of the STN are enveloped by fibers of the internal capsule, which separates this nucleus laterally from the GP. Postero-medially, the STN is very close to the red nucleus. The ventral borders of the STN are the cerebral peduncle and the substantia nigra. Dorsally, the STN has a border with the fasciculus lenticularis, which separates the STN from the ventral thalamus.

Several fiber tracts course near the borders of the STN. The subthalamic fasciculus consists of fibers that interconnect the STN and GP. This fiber bundle arises from the inferolateral border of the STN (Fig. 2).

The ansa lenticularis consists of fibers from the globus pallidus internus (GPI) that project toward the thalamus. It originates mainly from the lateral portion of the GPi, coursing in a medial, ventral, and rostral direction and sweeping anteriorly around the posterior limb of the internal capsule. This tract arises from the medial aspect of the GPi, perforates the internal capsule, and forms a bundle ventral to the zona incerta. Although some fibers
from the lenticular fasciculus are dorsal to the STN, most of this tract courses rostral to the nucleus. Fiber tracts lying posterior to the STN include the medial lemniscus, spinothalamic tract, and trigeminothalamic tract (Fig. 2).

In particular, the dorsal aspects of the lateral portion of the rostral two-thirds and the caudal one-third of the nucleus are anatomically related to the motor circuits. Subthalamic afferent fibers, corticosubthalamic projections, and most of the cortical afferents to the STN arise from the primary motor cortex, supplementary motor area, pre-supplementary motor area, and premotor area (Fig. 4).

The fibers traveling between the red nucleus and STN are known as the habenular commissure at midline sections of the brain. The mammillary body is located anterior to the STN. The mammillothalamic pathway is located anterosuperior to the STN (Fig. 4).

**Atlas-Based Localization of the Subthalamic Region**

Using the 3 spatial MRI planes and applying the anatomical knowledge acquired from the cadaveric dissections, we can localize the subthalamic region. This region is located ventral to the thalamus, medial to the internal capsule, and lateral and caudal to the hypothalamus. The nuclei found within the subthalamic region include the STN and zona incerta. The STN has a very close relationship with the substantia nigra and the red nucleus (Fig. 5).

**Discussion**

The STN is a small, lens-shaped nucleus in the brain. The STN is part of the basal ganglia system and is located ventral to the thalamus, dorsal to the substantia nigra, and medial to the internal capsule. It was first described by Jules Bernard Luys in 1865, and the terms corpus luysi and Luys body are still sometimes used. The STN is surrounded by dense bundles of myelinated fibers. Dorsally the STN is bordered by a portion of the fasciculus lenticularis and the zona incerta, which separate this nucleus from the ventral thalamus. As a consequence, the STN does not have sharp borders with the surrounding structures. Hence, the dissection is very difficult in this intricate region because of the challenge involved in calculating any anatomical measurement.

The volume of the STN is 40 mm in humans. The relationship between the volume of the STN and the total volume of the brain is proportionally similar in all humans.
Chronic stimulation of the STN, called deep brain stimulation (DBS), is used to treat patients with PD. The first cells to be stimulated are the terminal arborizations of afferent axons; the stimulation modifies the activity of subthalamic neurons.11 The function of the STN is unknown, but current theories present it as a component of the basal ganglia control system, which may perform action selection. Dysfunction of the STN has also been shown to increase impulsivity in individuals presented with two equally rewarding stimuli. The STN is populated mainly by projection neurons.

The first intracellular electrical recordings of subthalamic neurons were performed using sharp electrodes in a rat slice preparation.1 Several recent studies have focused on the autonomous pace-making ability of the subthalamic neurons. These neurons are often referred to as “fast-spiking pacemakers.”

The connection of the lateral pallidum with the STN is part of the basal ganglia. The activity of the medial pallidum is influenced by afferent signals from the lateral pallidum and the STN. The STN sends axons to another regulator region: the pedunculopontine complex. The lateropallido-subthalamic system is thought to have a key role in the regulation of movement.
role in the generation of the patterns of activity seen in PD.\textsuperscript{9}

In clinical practice, DBS of the STN is a promising new surgical option for the treatment of advanced PD. The marked clinical benefits obtained in these severely disabled patients outweigh the adverse effects.\textsuperscript{4} Accurate positioning of the electrodes allows the effects of stimulation to be confined to sensorimotor circuits.\textsuperscript{8}

Conclusions

The fiber dissection technique supports the presence of the subthalamic region as an integrative network in humans and offers the potential to aid in understanding the impacts of DBS surgery of the STN in patients with PD. Further research is needed to delineate definitively the role of the STN in the integrative process. Fiber dissections, done in conjunction with electrophysiological visualization or other techniques, offer confirmatory evidence that can lead to improvements in atlas-based localization of the subthalamic region.

References


Author Contributions

Conception and design: Akakın, Rhoton. Acquisition of data: Yılmaz, Rhoton. Analysis and interpretation of data: Kılıç, Rhoton.

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