# Cytoarchitectonic Mapping and Ultrahigh-Resolution 3D Reconstruction of the Bed Nucleus of Stria Terminalis

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**Introduction/motivation:** High-resolution brain atlases are a tool to find out more about human brain organization and its functions. Step by step each region of the brain has been mapped within a long-term effort to achieve this aim, and maps have been made available to public (Amunts and Zilles, 2015). The ongoing research focuses on the bed nucleus of the stria terminalis. The bed nucleus gets inputs from amygdala and hippocampus and has efferent connections to the hypothalamic region or the brainstem (Heimer and van Hoesen, 2006). The bed nucleus is involved in cortico-subcortical circuits affecting emotional processes such as fear and anxiety response, stress or motivation (Heimer and van Hoesen, 2006; Alvarez et al., 2011). The aim of this project is to delineate the bed nucleus of the stria terminalis in ten postmortem human brains, and to generate probability maps in stereotaxic space, which consider interindividual variability in size and localization of this brain region.

**Methods**: Ten postmortem brains, five male and five female, were fixed, paraffin-embedded and serially sectioned in coronal plane. Every 15th section (each 20 µm thick) was mounted and silver-stained for cell bodies (Merker, 1983). Histological processing was previously described in detail (Amunts et al., 1999). The sections were digitized for tracing the structures of the bed nucleus and the subsequent 3D-reconstruction. The delineation is based on cytoarchitectonic criteria, which enable to distinguish the bed nucleus of the stria terminalis from its neighbouring structures. Criteria include the shape, size or density of the neurons, as well as the density and distribution of glial cells. When the mapping is finished in all ten brains, the bed nucleus will be 3D reconstructed, registered to the MNI (Montreal Neurological Institute) single-subject brain template and then superimposed. This leads to so-called probability maps, showing the frequency of the bed nucleus in each voxel of the MNI reference space with values ranging from 0 to 100% in a certain region (Amunts and Zilles, 2015).

**Results**: The bed nucleus of the stria terminalis (BST) is located in the basal forebrain, close to the striatum and the lateral ventricles (Figures 1A,B). The bed nucleus is divided into two major subnuclei, the medial (BSTM) and the lateral bed nucleus of the stria terminalis (deOlmos, 2004; Heimer and van Hoesen, 2006).

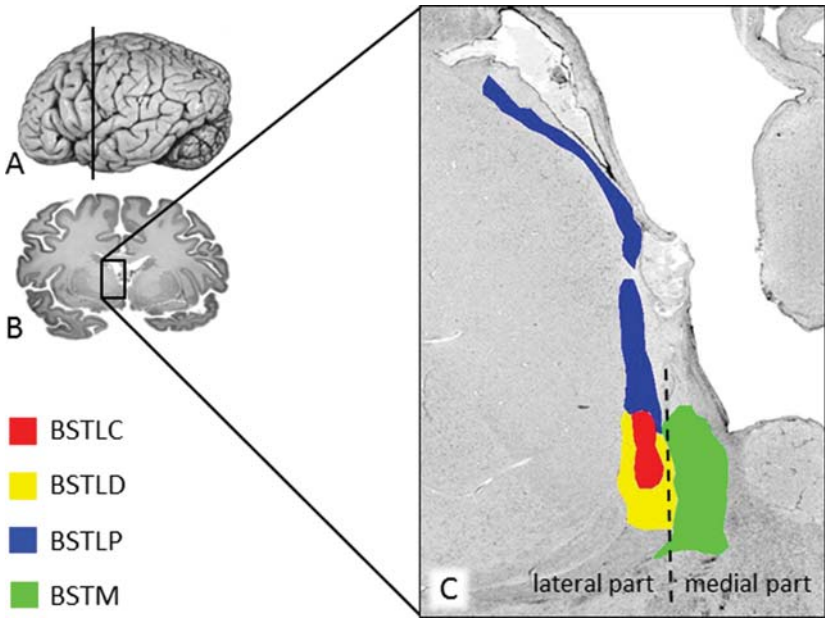


**FIGURE 1: (A)** Lateral view of a postmortem brain, **(B)** Silver-stained coronal section at the level marked in a, shortly after the decussation of the anterior commissure, **(C)** Magnification of the region of interest enclosed in black in b. Four different subdivisions of the bed nucleus of the stria terminalis (BST) were delineated: Three regions of the lateral part, i.e., BSTLC (red)—latero-central part. BSTLD (yellow)—latero-dorsal part, BSTLP (blue)—latero-posterior part and the medial part—BSTM (green) of the BST are shown.

The results show that the lateral BST is further subdivided into three parts (Figure 1C): The laterocentral part (BSTLC) consists of triangular and fusiform neurons and is surrounded by a cell-poor area. In coronal sections the BSTLC appears at the level of the decussating anterior commissure. It is in most sections enclosed by the latero-dorsal subdivision (BSTLD), which is characterized by frequently appearing islets, consisting of cell aggregates without any particular orientation of the neurons. Finally, the lateroposterior part (BSTLP) consists of smaller, lightly stained neurons as well as some bigger darkly stained neurons. This subdivision contains a substantial number of stria terminalis fibres, as it also extends dorsally towards the Nucleus caudatus. The BSTLP appears first shortly after the decussation of the anterior commissure in coronal sections and replaces the other subdivisions gradually. The BSTM mainly consists of small and densely packed neurons, but also contains larger more darkly stained neurons of various shapes, which leads to a heterogeneous appearance.

**Discussion**: Our results show four different subdivisions of the bed nucleus of the stria terminalis (BST), which were delineated according to their cytoarchitecture. Two examples regarding the cytoarchitecture as well as a functional aspect shall be briefly discussed in this passage: The BST as a whole was divided into a lateral and medial subnucleus, following the suggestions of Heimer and van Hoesen (2006), Heimer et al. (1999), and deOlmos (2004). In the lateral BST, the encapsulated central BST is classified within the dorsolateral subdivision of the BST. Avoiding one additional hierarchical step the BSTLC was considered as a part of the lateral subnucleus in this research project, equal to the other subdivisions, BSTLD and BSTLP.

On a functional level authors state, that the encapsulated central part of the BST is bigger in male than in female brains and it is responsible for sexual differentiation (Chung et al., 2002). Whether this sexual dimorphism can be confirmed will be answered as soon as all ten brains are reconstructed.

By obtaining probability maps of the bed nucleus of the stria terminalis with its distinct subdivisions will be one step forward, to achieve the overall goal of building a precise atlas of the human brain.

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