Cytoarchitectonic mapping, 3D-reconstruction and texture analysis of the human bed nucleus of the stria terminalis

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The bed nucleus of the stria terminalis (BST) is a basal forebrain structure mainly involved in anxiety disorders and stress response.¹ Despite its overall size of a few millimeters only, literature suggests that its subdivisions differ in connectivity and function.¹ Therefore, this study investigates the microstructure and extent of the subdivisions not only the BST itself. Ten postmortem brains (five male, five female) were fixed in formalin, paraffin-embedded, coronally sectioned and stained for cell bodies.² Identification of the bed nucleus and its subdivisions in serial sections followed criteria based on each region's particular cytoarchitectonic pattern. Four subdivisions of the bed nucleus were identified (Fig. 1): a central (BSTC), dorsal (BSTD), medial (BSTM) and posterior (BSTP) part. These structures were delineated over their whole extent, and 3D-reconstructed. Cytoarchitecture was studied by texture analysis, using a gray-level co-occurrence matrix,³ confirming the structural differences among the four subdivisions by showing distinct values of textural features, such as contrast, energy, homogeneity, or correlation. Probabilistic maps of the whole BST were generated by transferring individual maps to the MNI template brains Colin-27 and ICBM-152² to show the variability among the ten brains (Fig. 2a). A surface-based high-resolution 3Dreconstruction of the BST in the BigBrain⁴, a 3D model of the human brain, was calculated to visualize the complex shape of the BST and its subdivisions with high anatomical detail (Fig. 2b). These histology-based maps in 3D serve as a spatial and structural reference for in vivo neuroimaging findings, neuroscientific research questions and clinical studies targeting anxiety or stress-related diseases. It will enable to better distinguish the specific contributions of different subcortical structures. The probabilistic maps and the high-resolution maps in the BigBrain will be made publicly available via EBRAINS (https://ebrains.eu/service/human-brainatlas/).



Fig. 1: (a) Location of the bed nucleus of the stria terminalis in a coronal histological section stained for cell bodies. **(b)** Region of interest (rectangle in a) showing the shape of the bed nucleus and its four subdivisions: central part (BSTC), dorsal part (BSTD), medial part (BSTM) and posterior part (BSTP). Scalebar 2mm. **(c)** The four subdivisions and their specific cytoarchitectonic pattern. Asterisks show characteristic cell clusters in BSTD. Scalebar 200µm. Abbreviations: ac – anterior commissure, BST – bed nucleus of the stria terminalis, cc – corpus callosum, Cd – Nucleus caudatus, fx – fornix, GP – Globus pallidus, Hyp – Hypothalamus, ic – internal capsule, ot – optic tract, LV – lateral ventricle, P – Putamen, VP – Ventral pallidum.



Fig. 2: (a) Probabilistic maps of the whole BST in coronal, sagittal and axial planes in the MNI single subject template brain Colin-27. Warm colors represent high overlap of the ten brains, cold colors resemble an overlap of only a small number of brains. **(b)** Shape and arrangement of the 3D-reconstructed BST and its subdivisions.

References

¹Avery, S. N., Clauss, J. A., & Blackford, J. U. (2016). The human BNST: functional role in anxiety and addiction. *Neuropsychopharmacology*, *41*(1), 126-141.

²Amunts, K., H. Mohlberg, S. Bludau and K. Zilles (2020). "Julich-Brain: A 3D probabilistic atlas of the human brain's cytoarchitecture." <u>Science</u> **369**(6506): 988-992.

³Haralick, R. M., K. Shanmugam and I. H. Dinstein (1973). "Textural features for image classification." <u>IEEE Transactions on systems, man, and cybernetics</u>(6): 610-621.

⁴Amunts, K., Lepage, C., Borgeat, L., Mohlberg, H., Dickscheid, T., Rousseau, M.É., Bludau, S., Bazin, P.L., Lewis, L.B., Oros-Peusquens, A.M. and Shah, N.J., 2013. BigBrain: an ultrahigh-resolution 3D human brain model. *Science*, *340*(6139), pp.1472-1475. <u>https://doi.org/10.1126/science.1235381</u>