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What is the bed nucleus of the stria terminalis?

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What exactly is this bed nucleus of the stria terminalis? This is a question that I, and possibly all of my colleague neuroscientists with interest in this region of the brain, get on a regular basis. Unfortunately, the simplest questions are often the most difficult to answer.

Firstly, what's in a name? Researchers have failed to reach consensus on whether "BST" or "BNST" is the most effective acronym for their structure of interest. It seems there is little hope for clarification, as there is no scientific or grammatical justification using which we might choose one or the other. To our chagrin, both will probably continue to be commonly used. A description of the BST [sic] should start by reporting that it is a cluster of about 12 nuclei surrounding the caudal part of the anterior commissure, deep in the cerebral hemispheres. The exact number of BST nuclei varies depending on the criteria used, which are, at the moment, mostly anatomical. This may change in the future with more precise and localized permanent or reversible lesion approaches.

The BST is so named because it is located at one extremity of the stria terminalis, a bundle of axons that connects it with the amygdaloid nuclei. Although work is still needed to fully understand the function (s) of the BST, extensive anatomical studies of its connectivity suggest that it is a relay center within neurocircuits coordinating the activity of autonomic, neuroendocrine, and somatic motor systems into fully organized physiological functions and behaviours (Dong et al., 2001a,b; Dong and Swanson, 2003, 2004a, b, 2006a, b, c; Hasue and Shammah-Lagnado, 2002; Li and Kirouac, 2008; McDonald et al.,1999; Prewitt and Herman, 1998; Rodaros et al., 2007; Saggu and Lundy, 2007; Shin et al., 2008; Wood and Swann, 2005). Altogether, the BST seems to be a coordinating and relay center where descending cortical information meets ascending interoceptive and exteroceptive information regarding homeostatic states or potential changes in homeostasis. Information likely flows into the BST from exteroceptive (main and accessory olfactory, touch and nociception, gustatory) or interoceptive (energy and fluid levels, tissue damage, sexual hormone levels) sources through all central nervous system levels (from cortical to brain stem and spinal cord). The BST then has widespread descending projections to motor regions of the hindbrain that may trigger or contribute to the elaboration of coordinated physiological and behavioural responses necessary for a well-balanced homeostasis.

The BST can be roughly divided into anterior and posterior subdivisions, each containing several nuclei, which can be identified based on their projection pattern and neurochemical identity (Cassell et al., 1986; Day et al., 1999; Ju and Swanson, 1989; Ju et al., 1989; Larriva-Sahd, 2004, 2006; McDonald,1983; Moga et al.,1989; Veinante and Freund-Mercier, 1997). The anterior group (BSTant) seems to specialize in energy balance whereas the

posterior group (BSTpost) may contribute more to reproduction and defense. However, the anterior and posterior BST are highly interconnected, ruling out unrelated or distinct functions for the two general areas.

Although the BST is a relatively neglected structure of the brain with respect to physiological and behavioural studies, the available data somewhat confirms the predictions made from the anatomy. To date, lesions (reversible or irreversible) or pharmacological manipulations of the BST suggest roles in the physiology of fear, food intake, social behaviours, pain, and goal-directed behaviours and the associated pathophysiological states such as anxiety, anorexia, and addiction (Ciccocioppo et al., 2003; Colussi-Mas et al., 2005; Crown et al., 2000; Delfs et al., 2000; Deyama et al., 2007, 2008, 2009; Dumont et al., 2005; Dunn and Williams, 1995; Epping-Jordan et al., 1998; Erb and Stewart,1999; Fendt et al., 2003; Gewirtz et al.,1998; Jasnow et al., 2004; Lee and Davis, 1997; Leri et al., 2002; Liu et al., 2009; Nakagawa et al., 2005; Sajdyk et al., 2008; Sullivan et al., 2004; Walker and Davis, 1997; Walker et al., 2000; Wang et al., 2001).

In the present special issue of *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, seven groups of scientists generously contributed their time in reviewing their work and sharing their thoughts on their work on the BST, in addition to providing new and exciting data. In the first article, Walker et al. provide solid evidence that the BST manages stimuli associated with potential and non-imminent threats in contrast (or rather in complement) with the amygdaloid nuclei, which are critical for pairing unconditional stimuli with immediate threats. Along this line, Hammack et al. demonstrate both the complexity of serotoninergic modulation of BST neurons activity and how it changes in the face of stress and anxiety. Amir and Stewart next review their work on the regulation of the clock gene PER2 in the BST and the central amygdala, and discuss the key role of the BST – in particular the oval region – in circadian rhythms. Interestingly, they suggest that regulation of PER2 in the BST influences motivated behaviours in rodents. McElligot et al. gathered their work on excitatory transmission and plasticity of glutamate BST synapses with a special focus on the effects of drugs of abuse or stress on these synapses. On the other side of the engram, Sanna et al. discuss their recently reported studies of the intrinsic plasticity of BST neurons in animals chronically treated with drugs of abuse. Furthermore, Jalabert et al. review results from their respective work showing that the BST provides a major regulatory input to midbrain dopamine neurons, consistent with the role of the BST in goal-directed behaviours and the pathophysiology of addiction. Finally, Poulin et al. provide an important new set of neurochemical data that characterizes the endogenous opioid system of the BST, its specific distribution, and co-localization with immunohistochemical markers for the classic neurotransmitters GABA and glutamate.

We hope this special issue of *Progress in Neuro-Psychopharmacology and Biological Psychiatry* will trigger interest and excitement in this complex and intriguing region of the forebrain, and will prompt the reader to discover or revisit anatomical and physiological studies of the BST.

References

Cassell MD, Gray TS, Kiss JZ. Neuronal architecture in the rat central nucleus of the amygdala: a cytological, hodological, and immunocytochemical study. J Comp Neurol. 1986; 246:478–99. [PubMed: 2422231]

Ciccocioppo R, Fedeli A, Economidou D, Policani F, Weiss F, Massi M. The bed nucleus is a neuroanatomical substrate for the anorectic effect of corticotropin-releasing factor and for its reversal by nociceptin/orphanin FQ. J Neurosci. 2003; 23:9445–51. [PubMed: 14561874]

Colussi-Mas J, Panayi F, Scarna H, Renaud B, Berod A, Lambas-Senas L. Blockade of beta-adrenergic receptors prevents amphetamine-induced behavioural sensitization in rats: a putative role of the bed nucleus of the stria terminalis. Int J Neuropsychopharmacol. 2005; 8:569–81. [PubMed: 15836801]

Crown ED, King TE, Meagher MW, Grau JW. Shock-induced hyperalgesia: III. Role of the bed nucleus of the stria terminalis and amygdaloid nuclei. Behav Neurosci. 2000; 114:561–73. [PubMed: 10883806]

Day HE, Curran EJ, Watson SJ Jr, Akil H. Distinct neurochemical populations in the rat central nucleus of the amygdala and bed nucleus of the stria terminalis: evidence for their selective activation by interleukin-1beta. J Comp Neurol. 1999; 413:113–28. [PubMed: 10464374]

Delfs JM, Zhu Y, Druhan JP, Aston-Jones G. Noradrenaline in the ventral forebrain is critical for opiate withdrawal-induced aversion. Nature. 2000; 403:430–4. [PubMed: 10667795]

Deyama S, Nakagawa T, Kaneko S, Uehara T, Minami M. Involvement of the bed nucleus of the stria terminalis in the negative affective component of visceral and somatic pain in rats. Behav Brain Res. 2007; 176:367–71. [PubMed: 17101179]

Deyama S, Katayama T, Ohno A, Nakagawa T, Kaneko S, Yamaguchi T, et al. Activation of the beta-adrenoceptor-protein kinase A signaling pathway within the ventral bed nucleus of the stria terminalis mediates the negative affective component of pain in rats. J Neurosci. 2008; 28:7728–36. [PubMed: 18667605]

Deyama S, Katayama T, Kondoh N, Nakagawa T, Kaneko S, Yamaguchi T, et al. Role of enhanced noradrenergic transmission within the ventral bed nucleus of the stria terminalis in visceral pain-induced aversion in rats. Behav Brain Res. 2009; 197:279–83. [PubMed: 18793681]

Dong HW, Swanson LW. Projections from the rhomboid nucleus of the bed nuclei of the stria terminalis: implications for cerebral hemisphere regulation of ingestive behaviors. J Comp Neurol. 2003; 463:434–72. [PubMed: 12836178]

Dong HW, Swanson LW. Organization of axonal projections from the anterolateral area of the bed nuclei of the stria terminalis. J Comp Neurol. 2004a; 468:277–98. [PubMed: 14648685]

Dong HW, Swanson LW. Projections from bed nuclei of the stria terminalis, posterior division: implications for cerebral hemisphere regulation of defensive and reproductive behaviors. J Comp Neurol. 2004b; 471:396–433. [PubMed: 15022261]

Dong HW, Swanson LW. Projections from bed nuclei of the stria terminalis, anteromedial area: cerebral hemisphere integration of neuroendocrine, autonomic, and behavioral aspects of energy balance. J Comp Neurol. 2006a; 494:142–78. [PubMed: 16304685]

Dong HW, Swanson LW. Projections from bed nuclei of the stria terminalis, dorsomedial nucleus: implications for cerebral hemisphere integration of neuroendocrine, autonomic, and drinking responses. J Comp Neurol. 2006b; 494:75–107. [PubMed: 16304681]

Dong HW, Swanson LW. Projections from bed nuclei of the stria terminalis, magnocellular nucleus: implications for cerebral hemisphere regulation of micturition, defecation, and penile erection. J Comp Neurol. 2006c; 494:108–41. [PubMed: 16304682]

Dong HW, Petrovich GD, Swanson LW. Topography of projections from amygdala to bed nuclei of the stria terminalis. Brain Res Brain Res Rev. 2001a; 38:192–246. [PubMed: 11750933]

Dong HW, Petrovich GD, Watts AG, Swanson LW. Basic organization of projections from the oval and fusiform nuclei of the bed nuclei of the stria terminalis in adult rat brain. J Comp Neurol. 2001b; 436:430–55. [PubMed: 11447588]

Dumont EC, Mark GP, Mader S, Williams JT. Self-administration enhances excitatory synaptic transmission in the bed nucleus of the stria terminalis. Nat Neurosci. 2005; 8:413–4. [PubMed: 15735642]

Dunn JD, Williams TJ. Cardiovascular responses to electrical stimulation of the bed nucleus of the stria terminalis. J Comp Neurol. 1995; 352:227–34. [PubMed: 7721991]

Epping-Jordan MP, Markou A, Koob GF. The dopamine D-1 receptor antagonist SCH 23390 injected into the dorsolateral bed nucleus of the stria terminalis decreased cocaine reinforcement in the rat. Brain Res. 1998; 784:105–15. [PubMed: 9518570]

Erb S, Stewart J. A role for the bed nucleus of the stria terminalis, but not the amygdala, in the effects of corticotropin-releasing factor on stress-induced reinstatement of cocaine seeking. J Neurosci. 1999; 19:RC35. [PubMed: 10516337]

Fendt M, Endres T, Apfelbach R. Temporary inactivation of the bed nucleus of the stria terminalis but not of the amygdala blocks freezing induced by trimethylthiazoline, a component of fox feces. J Neurosci. 2003; 23:23–8. [PubMed: 12514197]

Gewirtz JC, McNish KA, Davis M. Lesions of the bed nucleus of the stria terminalis block sensitization of the acoustic startle reflex produced by repeated stress, but not fear-potentiated startle. Prog Neuropsychopharmacol Biol Psychiatry. 1998; 22:625–48. [PubMed: 9682277]

Hasue RH, Shammah-Lagnado SJ. Origin of the dopaminergic innervation of the central extended amygdala and accumbens shell: a combined retrograde tracing and immunohistochemical study in the rat. J Comp Neurol. 2002; 454:15–33. [PubMed: 12410615]

Jasnow AM, Davis M, Huhman KL. Involvement of central amygdalar and bed nucleus of the stria terminalis corticotropin-releasing factor in behavioral responses to social defeat. Behav Neurosci. 2004; 118:1052–61. [PubMed: 15506887]

Ju G, Swanson LW. Studies on the cellular architecture of the bed nuclei of the stria terminalis in the rat: I. Cytoarchitecture. J Comp Neurol. 1989; 280:587–602. [PubMed: 2708568]

Ju G, Swanson LW, Simerly RB. Studies on the cellular architecture of the bed nuclei of the stria terminalis in the rat: II. Chemoarchitecture. J Comp Neurol. 1989; 280:603–21. [PubMed: 2468695]

Larriva-Sahd J. Juxtacapsular nucleus of the stria terminalis of the adult rat: extrinsic inputs, cell types, and neuronal modules: a combined Golgi and electron microscopic study. J Comp Neurol. 2004; 475:220–37. [PubMed: 15211463]

Larriva-Sahd J. Histological and cytological study of the bed nuclei of the stria terminalis in adult rat. II. Oval nucleus: extrinsic inputs, cell types, neuropil, and neuronal modules. J Comp Neurol. 2006; 497:772–807. [PubMed: 16786552]

Lee Y, Davis M. Role of the hippocampus, the bed nucleus of the stria terminalis, and the amygdala in the excitatory effect of corticotropin-releasing hormone on the acoustic startle reflex. J Neurosci. 1997; 17:6434–46. [PubMed: 9236251]

Leri F, Flores J, Rodaros D, Stewart J. Blockade of stress-induced but not cocaine-induced reinstatement by infusion of noradrenergic antagonists into the bed nucleus of the stria terminalis or the central nucleus of the amygdala. J Neurosci. 2002; 22:5713–8. [PubMed: 12097523]

Li S, Kirouac GJ. Projections from the paraventricular nucleus of the thalamus to the forebrain, with special emphasis on the extended amygdala. J Comp Neurol. 2008; 506:263–87. [PubMed: 18022956]

Liu TL, Chen DY, Liang KC. Post-training infusion of glutamate into the bed nucleus of the stria terminalis enhanced inhibitory avoidance memory: an effect involving norepinephrine. Neurobiol Learn Mem. 2009; 91:235–42. [PubMed: 19041726]

McDonald AJ. Neurons of the bed nucleus of the stria terminalis: a golgi study in the rat. Brain Res Bull. 1983; 10:111–20. [PubMed: 6824959]

McDonald AJ, Shammah-Lagnado SJ, Shi C, Davis M. Cortical afferents to the extended amygdala. Ann N Y Acad Sci. 1999; 877:309–38. [PubMed: 10415657]

Moga MM, Saper CB, Gray TS. Bed nucleus of the stria terminalis: cytoarchitecture, immunohistochemistry, and projection to the parabrachial nucleus in the rat. J Comp Neurol. 1989; 283:315–32. [PubMed: 2568370]

Nakagawa T, Yamamoto R, Fujio M, Suzuki Y, Minami M, Satoh M, et al. Involvement of the bed nucleus of the stria terminalis activated by the central nucleus of the amygdala in the negative affective component of morphine withdrawal in rats. Neuroscience. 2005; 134:9–19. [PubMed: 15939543]

Prewitt CM, Herman JP. Anatomical interactions between the central amygdaloid nucleus and the hypothalamic paraventricular nucleus of the rat: a dual tract-tracing analysis. J Chem Neuroanat. 1998; 15:173–85. [PubMed: 9797074]

Rodaros D, Caruana DA, Amir S, Stewart J. Corticotropin-releasing factor projections from limbic forebrain and paraventricular nucleus of the hypothalamus to the region of the ventral tegmental area. Neuroscience. 2007; 150:8–13. [PubMed: 17961928]

Saggu S, Lundy RF. Forebrain neurons that project to the gustatory parabrachial nucleus in rat lack glutamic acid decarboxylase. Am J Physiol Regul Integr Comp Physiol. 2007; 294:R52–7. [PubMed: 17989138]

Sajdyk T, Johnson P, Fitz S, Shekhar A. Chronic inhibition of GABA synthesis in the bed nucleus of the stria terminalis elicits anxiety-like behavior. J Psychopharmacol. 2008; 22:633–41. [PubMed: 18308797]

Shin JW, Geerling JC, Loewy AD. Inputs to the ventrolateral bed nucleus of the stria terminalis. J Comp Neurol. 2008; 511:628–57. [PubMed: 18853414]

Sullivan GM, Apergis J, Bush DE, Johnson LR, Hou M, Ledoux JE. Lesions in the bed nucleus of the stria terminalis disrupt corticosterone and freezing responses elicited by a contextual but not by a specific cue-conditioned fear stimulus. Neuroscience. 2004; 128:7–14. [PubMed: 15450349]

Veinante P, Freund-Mercier MJ. Distribution of oxytocin- and vasopressin-binding sites in the rat extended amygdala: a histoautoradiographic study. J Comp Neurol. 1997; 383:305–25. [PubMed: 9205043]

Walker DL, Davis M. Double dissociation between the involvement of the bed nucleus of the stria terminalis and the central nucleus of the amygdala in startle increases produced by conditioned versus unconditioned fear. J Neurosci. 1997; 17:9375–83. [PubMed: 9364083]

Walker JR, Ahmed SH, Gracy KN, Koob GF. Microinjections of an opiate receptor antagonist into the bed nucleus of the stria terminalis suppress heroin self-administration in dependent rats. Brain Res. 2000; 854:85–92. [PubMed: 10784110]

Wang X, Cen X, Lu L. Noradrenaline in the bed nucleus of the stria terminalis is critical for stress-induced reactivation of morphine-conditioned place preference in rats. Eur J Pharmacol. 2001; 432:153–61. [PubMed: 11740951]

Wood RI, Swann JM. The bed nucleus of the stria terminalis in the Syrian hamster: subnuclei and connections of the posterior division. Neuroscience. 2005; 135:155–79. [PubMed: 16084647]