World Journal of Neurology

Online Submissions: http://www.wjgnet.com/esps/
wjneurol@wjgnet.com
doi:10.5316/wjn.v3.i2.4

World J Neurol 2013 June 28; 3(2): 4-6
ISSN 2218-6212 (online)

EDITORIAL

Anatomizing the "King of Neurosciences"

Ioannis N Mavridis

Ioannis N Mavridis, Medical office of the Command of the Hellenic Navy General Staff (Naval Hospital of Athens), 15561 Athens, Greece
Author contributions: Mavridis IN solely contributed to this paper.
Correspondence to: Ioannis N Mavridis, MD, PhD, Medical office of the Command of the Hellenic Navy General Staff (Naval Hospital of Athens), Mesogion Av. 229, Cholargos, 15561 Athens, Greece. pap-van@otenet.gr
Telephone: +30-697-8327199 Fax: +30-210-2833600
Received: February 10, 2013 Revised: March 19, 2013
Accepted: May 8, 2013
Published online: June 28, 2013

Abstract

The human nucleus accumbens (NA), a major part of the ventral striatum, is the area of continuity between the putamen and head of the caudate nucleus. It consists of two parts, a shell laterally and a core medially. The first is mainly connected to the limbic system and the second to the extrapyramidal motor system. The NA, a major pleasure center of the human brain, acts as a limbic-motor interface and is involved in several cognitive, emotional and psychomotor functions. It has a modulating function in the amygdala-basal ganglia-prefrontal cortex circuit. It is considered as the neural interface between motivation and action. Further, it is a principal modulator of the reward circuits and supplies motor expression to emotional responses. Such a clinical significance could easily explain the intense work taking place in the respective field of basic research. Its exceptional clinical importance justifies the title of the "King of Neurosciences" for this nucleus. Purpose of this editorial is to review the "informational paths" left behind by the few researchers who tried to explore the architecture (gross anatomy) of this 'kingdom'. The first anatomical study focused on this nucleus came from Neto *et al*. The most extensive study of the NA gross, imaging, stereotactic and neurosurgical anatomy so far, came from the research efforts of Mavridis *et al*.

Key words: Gross anatomy; Neurosciences; Neurosurgical anatomy; Nucleus accumbens; Stereotactic anatomy

Core tip: The human nucleus accumbens (NA), a major pleasure center of the brain, is a limbic-motor interface involved in several neurological and psychiatric disorders. It became recently a deep brain stimulation target for selected patients. Its exceptional clinical significance justifies its title as the "King of Neurosciences". Purpose of this editorial is to review the few studies who explored the NA gross anatomy. The first anatomical study focused on this nucleus came from Neto *et al*. The most extensive study of the NA gross, imaging, stereotactic and neurosurgical anatomy came from the research of Mavridis *et al*.

Mavridis IN. Anatomizing the "King of Neurosciences". *World J Neurol* 2013; 3(2): 4-6 Available from: URL: http://www.wjgnet.com/2218-6212/full/v3/i2/4.htm DOI: http://dx.doi.org/10.5316/wjn.v3.i2.4

THE HUMAN NUCLEUS ACCUMBENS

The human nucleus accumbens (NA), a major part of the ventral striatum, is the area of continuity between the putamen and head of the caudate nucleus[1]. It consists of two parts, a shell laterally and a core medially. The first is mainly connected to the limbic system and the second to the extrapyramidal motor system (Figure 1). NA's afferent connections include: hippocampus, frontal cortex, entorhinal cortex, amygdala, cingulate gyrus and thalamus. Its efferent connections include: striatum, globus pallidus, hypothalamus, prefrontal cortex, ventral tegmental area and substantia nigra. The principal neurotransmitters in NA circuits are

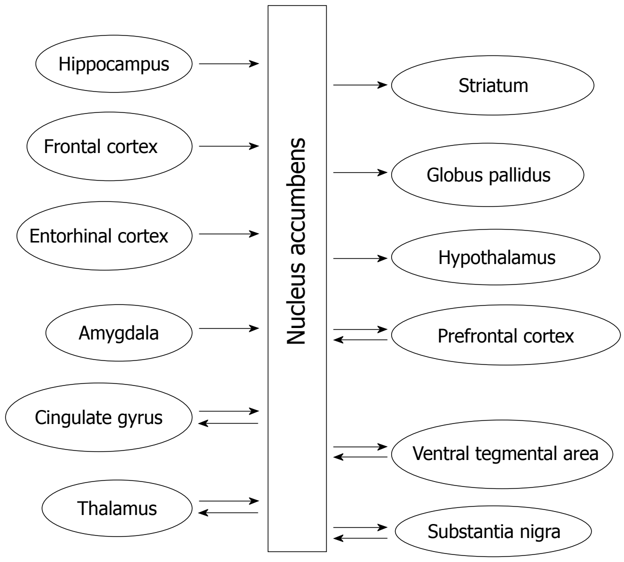

Figure 1 Nucleus accumbens connections. Schematic representation of the nucleus accumbens afferent and efferent connections within the human brain (modified from Mavridis[2]).

glutamic acid, dopamine and γ-aminobutyric acid (GABA)[2].

The NA, a major pleasure center of the human brain[2], acts as a limbic-motor interface and is involved in several cognitive, emotional and psychomotor functions[1]. It has a modulating function in the amygdala-basal ganglia-prefrontal cortex circuit. It is considered as the neural interface between motivation and action. Further, it is a principal modulator of the reward circuits and supplies motor expression to emotional responses[2]. The NA anatomical architecture and pathways, as well as the effect of different drugs on the NA have been studied on experimental animals.

"KING OF NEUROSCIENCES"

The human NA is involved in several neurological disorders including epilepsy, Parkinson's disease, Huntington's chorea, frontotemporal dementia, narcolepsy and spinocerebellar ataxia[2]. Given its great functional importance, it is not surprising that this nucleus is also involved in several psychiatric disorders such as obsessive-compulsive disorder, depression, Tourette syndrome, addiction, schizophrenia, bipolar disorder, attention-deficit/hyperactivity disorder, post-traumatic stress disorder and apathy[2]. Latest decade's advancements in Stereotactic Neurosurgery made the NA a deep brain stimulation target for selected patients mainly suffering from obsessive-compulsive disorder, depression and Tourette syndrome[2].

Such a clinical significance could easily explain the intense work taking place in the respective field of basic research. There are numerous neurochemical and neurobiological studies of the NA in the literature, usually focusing on neurons and neurotransmitters of this nucleus and its crucial connections. Moreover, there are several neuroimaging and some neuroanatomical studies of the human NA. The first are mainly magnetic resonance imaging (MRI) or functional MRI studies.

According to the above physiological and clinical data which aimed to light just the peak of the amazing iceberg, of the "Arctic Ocean of Neurosciences", called "human NA", I think that this exceptional nucleus rightfully deserves the crown of the "King of Neurosciences". Purpose of this editorial is to review the 'informational paths' left behind by the few researchers who tried to explore the architecture (gross anatomy) of this "kingdom".

GROSS ANATOMICAL STUDIES

Several animal studies have investigated the anatomy and physiology of the NA[1]. There are some studies that provided morphometric data of the human NA[1,3-7]. Methodologically, Yelnik *et al*[6] and Bardinet *et al*[7] used post-mortem brain MRIs (as well as dissections with cryomacrotome) for three-dimensional studying of the human basal ganglia. Xia *et al*[3] used T1-weighted high-resolution MRIs for studying the caudate nucleus (including findings about the NA). Ahsan *et al*[5] also used high-resolution MRIs for their volumetric study of the human basal ganglia and thalamus. Brabec *et al*[4] used anatomical dissections and MRIs for their volumetric study of the striatum. Neto *et al*[1] applied MRIs as well as coronal anatomical slices into cadaveric brains for their NA-focused study. Mavridis *et al*[8-11] used formalin-fixated cerebral hemispheres for studying NA stereotactic anatomy and morphometry and specific details of the NA deep brain stimulation (DBS) operative technique. They also used cerebral MRIs for studying NA stereotactic anatomy and morphometry[8,9], as well as MRIs from patients with Parkinson's disease[12].

Neto *et al*[1] studied the location, limits and size of the human NA and found the right NA to be wider than the left one. They reported that the precise limits of the NA were only possible to delimitate in the anatomical study and that the NA does not have a distinct signal intensity imaging, as well as no evidence of NA width or height variations along age and that this nucleus does not suffer any age-related atrophy as other brain structures. Brabec *et al*[4] reported absence of significant difference of the absolute volume of the caudate-accumbens complex between sides and gender. In contrast, Ahsan *et al*[5] found greater left NA.

Mavridis *et al*[9] found the definition of the NA limits with the caudate nucleus and putamen easier by MRI than by anatomical technique, specifically on T2-weighted MRIs due to the slightly more intense MR signal (remarkably similar to those of the cerebral cortex) that this nucleus presents compared to the caudate nucleus and putamen (and also compared to other nuclei such as the red or subthalamic nucleus). They also agreed with Neto *et al*[1] about the difficulty in establishing the rostral end of the NA relative to the caudate nucleus and putamen but found no such difficulty in transverse MRI sections.

They also found no statistically significant difference among side regarding the NA stereotactic coordinates and dimensions[8,9] and that the human NA extended superiorly above the intercommissural plane[11] and was paradoxically longer in the elderly[9]. Further, its maximum transverse dimension was greater in individuals with putamen microcysts (dilated perivascular spaces)[9] and the absolute value of its y' coordinate was greater in males[8]. The NA was morphometrically correlated neither with the striatum[9] nor with its cortical connections. However, they found significant correlations of the thickness of NA cortical connections, specifically: the orbitofrontal with the entorhinal cortex, the cingulate with the orbitofrontal cortex, the piriform with the orbitofrontal and entorhinal cortices[2].

In addition, Mavridis *et al*[8] found stereotactically standard areas in the NA (*e.g.*, G, H, M). Standard area M (Mavridis' area), based on a combined study of anatomic specimens and MRIs, which is defined by coordinates x = 6.0 mm, x' = 9.0 mm, y = 2.0 mm, y' = 2.0 mm, z = -0.8 mm, z' = -2.0 mm and has a 3.6 mm^2 surface, always consisted a NA part regardless of side (right-left) or gender (male-female). They also found that the human NA is smaller in patients with advanced Parkinson's disease (Mavridis' atrophy). The mean percentage reduction of its size was 11.77%[12].

Finally, Mavridis *et al*[2] studied anatomical details of the NA DBS surgical technique on cadavers, they found that the today used electrode target point for NA DBS missed the target in 8% of cases[11] and they proposed a safe navigation model ('port' model) for NA DBS[10] as well as new surgical approaches and anatomic landmarks for NA surgery[2].

CONCLUSION

In conclusion, the human NA, a major pleasure center of the human brain, is a limbic-motor interface involved in several neurological and psychiatric disorders. During the last decade, this nucleus is also a DBS target for selected patients. Its exceptional clinical significance justifies the title of the "King of Neurosciences" for this nucleus. There are few researchers who tried to explore the gross anatomy of this nucleus. The first anatomical study focused on this nucleus came from Neto *et al*[1]. The most extensive study of the NA gross, imaging, stereotactic and neurosurgical anatomy so far, came from the research efforts of Mavridis *et al*[2,8-12].

REFERENCES

1 **Neto LL**, Oliveira E, Correia F, Ferreira AG. The human nucleus accumbens: where is it? A stereotactic, anatomical and magnetic resonance imaging study. *Neuromodulation* 2008; **11**: 13-22 [PMID: 22150987 DOI: 10.1111/j.1525-1403.2007.00138.x]

2 **Mavridis IN.** [Stereotactic neurosurgical anatomy of the nucleus accumbens]- PhD Thesis. Athens: School of Medicine, National and Kapodistrian University of Athens, 2012: 42-59. Available from: URL: http://www.lib.uoa.gr/greylit/greylit.pl?i=CE8254B35CE35B06C2257A3100487A71

3 **Xia Y**, Bettinger K, Shen L, Reiss AL. Automatic segmentation of the caudate nucleus from human brain MR images. *IEEE Trans Med Imaging* 2007; **26**: 509-517 [PMID: 17427738 DOI: 10.1109/TMI.2006.891481]

4 **Brabec J**, Krásený J, Petrovický P. Volumetry of striatum and pallidum in man--anatomy, cytoarchitecture, connections, MRI and aging. *Sb Lek* 2003; **104**: 13-65 [PMID: 14577136]

5 **Ahsan RL**, Allom R, Gousias IS, Habib H, Turkheimer FE, Free S, Lemieux L, Myers R, Duncan JS, Brooks DJ, Koepp MJ, Hammers A. Volumes, spatial extents and a probabilistic atlas of the human basal ganglia and thalamus. *Neuroimage* 2007; **38**: 261-270 [PMID: 17851093 DOI: 10.1016/j.neuroimage.2007.06.004]

6 **Yelnik J**, Bardinet E, Dormont D, Malandain G, Ourselin S, Tandé D, Karachi C, Ayache N, Cornu P, Agid Y. A three-dimensional, histological and deformable atlas of the human basal ganglia. I. Atlas construction based on immunohistochemical and MRI data. *Neuroimage* 2007; **34**: 618-638 [PMID: 17110133 DOI: 10.1016/j.neuroimage.2006.09.026]

7 **Bardinet E**, Bhattacharjee M, Dormont D, Pidoux B, Malandain G, Schüpbach M, Ayache N, Cornu P, Agid Y, Yelnik J. A three-dimensional histological atlas of the human basal ganglia. II. Atlas deformation strategy and evaluation in deep brain stimulation for Parkinson disease. *J Neurosurg* 2009; **110**: 208-219 [PMID: 18976051 DOI: 10.3171/2008.3.17469]

8 **Mavridis I**, Boviatsis E, Anagnostopoulou S. Stereotactic anatomy of the human nucleus accumbens: from applied mathematics to microsurgical accuracy. *Surg Radiol Anat* 2011; **33**: 583-594 [PMID: 21437651 DOI: 10.1007/s00276-011-0804-z]

9 **Mavridis I**, Boviatsis E, Anagnostopoulou S. Anatomy of the human nucleus accumbens: a combined morphometric study. *Surg Radiol Anat* 2011; **33**: 405-414 [PMID: 21203764 DOI: 10.1007/s00276-010-0766-6]

10 **Mavridis I**, Anagnostopoulou S. The safest electrode trajectory for deep brain stimulation of the human nucleus accumbens: a stereotactic anatomic study. *Minim Invasive Neurosurg* 2011; **54**: 16-20 [PMID: 21506063 DOI: 10.1055/s-0030-1270516]

11 **Mavridis I**, Anagnostopoulou S. The human nucleus accumbens as a target for deep brain stimulation: anatomic study of electrode's target point and stereotactic coordinates. *Minim Invasive Neurosurg* 2009; **52**: 212-215 [PMID: 20077360 DOI: 10.1055/s-0029-1243240]

12 **Mavridis I,** Boviatsis E, Anagnostopoulou S. The human nucleus accumbens suffers parkinsonism-related shrinkage: a novel finding. *Surg Radiol Anat* 2011; **33**: 595-599 [PMID: 21404044 DOI: 10.1007/s00276-011-0802-1]

P- Reviewer El-Naggar MM
S- Editor Gou SX **L- Editor** A **E- Editor** Lu YJ