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MYSTERIOUS STAR IN THE BRAIN: ACCUMBENS NUCLEUS

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All current neuroanatomy data shows multiple brain centers on which our knowledge of their function and structure is still very limited. One such center is Nucleus Accumbens (Nac), which has been discovered, thanks to studies in recent years, to represent a crucial structure involved in emotional and motivational processes. Nucleus Accumbens have a mosaic organization, which consists of two different but interconnected departments, which gives it the appearance of its “Patch-Matrix”. A special feature of this brain structure is that it can be divided into two distinct areas, each with different functions and connections: a central core surrounded by an outer shell. The nervous circuit of Nucleus Accumbens presents two different projection areas due to the differences between accumbal shell and accumbal core. Dopamine is the neurotransmitter with the highest value at the Nucleus Accumbens level, being the first substance at this level that has attracted the attention of neuroscientists, due to its role in addiction and the natural reward system of the brain.

NAc is still a mystery to medicine today, because as many neurotransmitters as it hides, as much information. Instead, it represents a huge potential for everything that the medicine of the future means.

Keywords: Nucleus Accumbens, Patch-Matrix, Dopamine, Acetylcholine, Neurotransmiters.

INTRODUCTION

Nucleus accumbens is set up in an area of the brain called the basal forebrain. There is a nucleus accumbens in each cerebral hemisphere; it is situated between the caudate and putamen. The nucleus accumbens is considered part of the basal ganglia and also is the main component of the ventral striatum. The nucleus accumbens itself is separated into two anatomical components: the shell and the core. These two different areas have numerous connections, but may make different contributions to the functions of the nucleus accumbens. Nucleus Accumbens is also a bomb of neurotransmitters, neurotransmitters that have an essential role in the functions of this brain structure. The nervous pathways of dopamine and acetylcholine are interconnected with the Nucleus Accumbens pathways.

HISTORY

The term Nucleus Accumbens was first used in 1904 by Zihen, followed by a discussion between Kappers and Theunissen (1908), and Johnston (1913) in which arguments were made for the correct term Nucleus Accumbens. The two terms used were “nucleus accumbens septi”, a term suggested by Kappers and Theunissen, and “nucleus lateralis parolfactorius”, a term suggested by Johnston. The latest studies show, however, that the accumbens is an integral, but specialized, part of the striatal complex, closely related the caudate-putamen (striatum) and separate in function and composition from the septum.[1–3]

ORGANIZATION: “PATCH-MATRIX” AND ACCUMBAL CORE AND SHELL

Nucleus Accumbens is a cerebral structure with numerous connections and special morphological and molecular aspects. Thus, the way of organizing and dividing it is based on several criteria.

The similarities with the striatal tissue make Nucleus Accumbens have a mosaic organization, which consists of two different but interconnected departments, which gives it the appearance of its “Patch-Matrix”.[4] The patches are characterized by dense μ-opiate receptor-binding sites, while the matrix consists of weaker opiate receptor binding, a rich plexus of somatostatin fibers, strong calcium-binding protein immunoreactivity and a high acetylcholinesterase activity.[5]

The immunohistochemical distribution of certain markers such as enkephalin, calcium-binding protein, dopamine and substance P, reinforces the fact that the organization of Nucleus Accumbens is striosomal or “patch-matrix”.[6]

A special feature of this brain structure is that it can be divided into two distinct areas, each with different functions and connections: a central core surrounded by an outer shell.

From a morphological point of view, it has been discovered that the neurons in the two areas are different, even opposite. If at the accumbal core level there are pyramidal neurons, with fewer dendritic endings, at the level of the accumbal shell there are multipolar neurons, rich in nerve endings.[7]

Differences are also found at the molecular level, where it can be observed in the accumbal shell the predominance of neuroactive substances, such as dopamine, calretinin, serotonin and substance P. At the level of accumbal core there are mostly substances such as enkephalin, calbindin, $GABA_A$ receptors.

Even at the histological level, certain recent studies describe the special characteristics of accumbal shell. It has morphological, molecular and related elements similar to the surrounding anatomical structures, such as extended amygdala and striatal tissue. These similarities include immunohistochemical aspects, such as areas rich in opioid peptides, neurotensin and cholecystokinin, but also aspects of connection such as efferents to the lateral hypothalamus and afferents from the basolateral complex of the amygdala. The conclusion of the studies was that accumbal shell shares common elements with the striatum, but also with the extended amygdala.[8] Which can also make us understand why the initial controversy between the terms “nucleus accumbens septi” and “nucleus lateralis parolfactorius”.

It should be noted, however, that due to the complexity of this structure, both morphological and molecular, Nucleus Accumbens can present several levels of organization. In the latest studies it is shown that there is a possibility of organization according to the rostro-caudal differences of the structures in Nucleus Accumbens.

A BOMB OF NEUROTRANSMITERS

The nervous circuit of Nucleus Accumbens presents two different projection areas due to the differences between accumbal shell and accumbal core. The shell is projected at the level of the prefrontal and subcortical areas, including structures such as lateral hypothalamus and extended amygdala. The neural connections in the core end up projecting at the level of the premotor and additional motor areas.[9]

Nucleus Accumbens also features in dopamine circuits, one of the key neurotransmitters in this neural structure. The accumbal shell shows dopaminergic connections with structures such as ventromedial ventral pallidum, mediodorsal nucleus, prefrontal cortex and ventral tegmental area (VTA), which continue this route of dopamine up to the level of mesocortical sites. The accumbal core shows a different dopamine circuit, a circuit that includes the dorsolateral ventral pallidum. It continues the neurotransmitter circuit up to the subthalamic nucleus and substantia nigra, the origin of dopaminergic innervation of the striatum.

Dopamine is the neurotransmitter with the highest value at the Nucleus Accumbens level, being the first substance at this level that has attracted the attention of neuroscientists, due to its role in addiction and the natural reward system of the brain.[11,13] It has been shown that the shell is innervated by nerve fibers coming from the ventral tegmental area, while the core shows numerous afferents from the neurons in the substantia nigra, neurons that have effect on striatal neurons. Thus, it was hypothesized that the two structures of Nucleus Accumbens are related to nigrostriatal system and mesolimbic system.[14]

GABA and Glutamate neurons from this neural structure are another major element involved in the Nucleus Accumbens function. GABAergic neurons that are projecting to the ventral pallidum and globus pallidus presents an important role in schizophrenia because of the context-dependent arousal effect.[15] GABA injections have some effects on locomotion, and can cause hyperactivity or hypoactivity, depending on the doses that are administrated. Alterations in accumbal glutamate neurons can influence locomotion behavior too.[16]

Another important neurotransmitter in the Nucleus Accumbens is acetylcholine. This substance has two main pathways. Its first circuit is represented by a forebrain projection from the nucleus basalis magnocellularis to the basolateral amygdala. And the second circuit is represented by a hindbrain projection from the mesopontine cell groups to the VTA and substantia nigra that modulates accumbal DA neurons. These two have roles in some of the Nucleus Accumbens pathological activities, like drug relapse, psychosis and schizophrenia.[17–19]

CONCLUSIONS

Nucleus Accumbens is still a mystery to medicine today, because as many neurotransmitters as it hides, as much information. Instead, it represents a huge potential for everything that the medicine of the future means. Surgical interventions for this structure are intriguing, and can be the start of an era where stereotactic and functional neurosurgeons can change the view about neurodegenerative diseases and their treatment.

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