OLFACTORY SYSTEM – IMPLICATION FOR PARKINSON'S DISEASE

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Abstract: *Olfactory deficit is frequently encountered in the neurodegenerative diseases - Parkinson's disease and Alzheimer's disease. Neuropathological substrate of olfactory dysfunction in the neurodegenerative diseases is incompletely understood, but degenerative changes are found at different levels of the olfactory system, such as the olfactory epithelium, olfactory bulb, primary olfactory cortex.*

Cuvinte cheie: *deficit olfactiv, boli neurodegenerative, boala Parkinson*

Rezumat: *Deficitul olfactiv este frecvent întâlnit în bolile neurodegenerative – boala Parkinson, dar şi în boala Alzheimer. Substratul neuropatologic al disfuncţiei olfactive în bolile neurodegenerative este incomplet elucidat, însă modificări degenerative se întâlnesc la diferite nivele ale sistemului olfactiv, cum ar fi: epiteliul olfactiv, bulbul olfactiv, cortexul primar olfactiv.*

The olfactory system is an example of functional plasticity. The olfactory sensory information is processed at a central level through a complex mechanism.

The olfactory deficit was found in neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease.

The neuropathologic substratum of the olfactory dysfunction is incompletely elucidated, but it reveals degenerative changes at different levels of the olfactory system, such as the olfactory epithelium, the olfactory bulb, the primary olfactory cortex.

The sensorial olfactory neurons are disposed as patches at the level of the respiratory neuroepithelium.

Those neurons are bipolar cells whose dendrites have 3-50 cilia that are projected in the mucus, while the axons make synapses in the olfactory bulb.

At the level of the human olfactory neurons, almost 400 receptors are described, and an olfactory neuron responds to several odorised stimuli.

The first step in the translation of the olfactory system consists in the activation of the Gα olfactory that stimulates the adenylyl cyclase 3 and determines the production of cyclic adenosine monophosphate.

This trigger determines the opening of the Ca^{2+} channels with the penetrating of the Ca in cells and depolarization, followed by the opening of the Cl channels and the Cl efflux, which amplifies the depolarization of the sensory neurons.

The olfactory receptor neurons have a unique property of regeneration.

They are directly exposed to the action of the environment factors and represent a main entrance in the brain for the viruses and toxins.

The number of the sensorial neurons decreases with the age and especially over 65 years old.

The olfactory receptor neurons have glutamatergic mediation and send excitatory impulses to the olfactory bulb, where signals are sent to the olfactory cortex.

The olfactory bulb has a complex synaptic structure being a very important „site" of processing the olfactory information.

It has been suggested that the olfactory bulb may constitute the „olfactory thalamus". As the thalamus, the olfactory bulb is the final stage of processing the sensorial information before being transmitted to the cerebral cortex.

The olfactory neurons from the olfactory bulb, as well as the thalamic neurons, receive feedback from olfactory cortical areas and modulator impulses from the cerebral trunk.

The axons of the neurons from the olfactory bulb form the lateral olfactory tract that contains small myelinic fibres that end in the olfactory cortex.

The 51 area – the piriform cortex is the biggest olfactory area and is situated at the junction between the latero-caudal portion of the frontal lobe and the dorso-median portion of the temporal lobe.

The piriform cortex has a heterogeneous architecture and functionality.

Other primary olfactory areas are represented by the cortical anterior nuclei of the amygdale, the periamygdaloid cortex and the entorhinal cortex.

Between these areas, there are intracortical connections.

The olfactory cortex receives impulses from the cholinergic and monoaminergic neurons from hypothalamus, cerebral trunk, basal nuclei.

Neuroimaging PET studies highlight that the activation at the level of the piriform, entorhinal, orbitofrontal, amygdalian cortex, as an answer to the olfactory stimuli, is lower in the aged people than in the young people.

The most used method for smell identification is the UPSIT method.

The progressive deterioration of the olfactory function in the aged people reflects the neuronal loss in the olfactory bulb.

The olfactory bulb is affected in over 30% of the subjects without clinical signs of Parkinson's disease and in over 90% of those with clinical signs of Parkinson's disease.

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The early implication of the olfactory bulb and of the enteric nervous plexus in the Parkinson's disease is explained by a dual hypothesis regarding the presence of the Levy bodies.

It is supposed that a neurotropic pathogen enters the brain through the nasal airway with an anterograd progression to the temporal lobe, or through gastric airway with trans-synaptic transmission through the Meissner's plexus to the dorsal motor nucleus of the vagus.

The olfactory dysfunction is an early manifestation and precedes the motor signs of the Parkinson's disease in 70-100% of the patients.

Olfactory discrimination deficit is independent of the disease progression.

The functional MRI studies show the reduction of the activities in the olfactory areas in the early stages of the Parkinson's disease.

The olfaction is preserved in the patients with genetic parkinsonism, such as the mutation of the Parkin gene and the mutation of the DJ-1 .

This suggests that the pathology with Levy bodies is „necessary" for the development of the olfactory dysfunction in the Parkinson's disease.

Anosmia may be present also in other disorders with Levy bodies such as: dementia with Levy bodies, primary orthostatic hypotension, Alzheimer dementia.

Hyposmia is only rarely associated with parkinsonism in tauopathies, such as the progressive supranuclear paralysis or corticobasal degeneration.

The implication of the olfactory system may be a biomarker that precedes the motor manifestations from the Parkinson's disease.

Several studies reported an olfactory dysfunction in the early stages of the Parkinson's disease.

There were studies that analysed the relation between the olfactory dysfunction and the cardiovascular dysautonomia in the patients with Parkinson's disease.

Parkinson's disease causes not only motor disorders, such as: resting tremor, rigidity, bradykinesia and walking disorders, but also cognitive disorders, autonomic dysfunction, depression, sleep disorders, dementia.

The olfactory dysfunction is a non-motor sign important in Parkinson's disease. It precedes the motor symptoms.

The autonomic dysfunction significant from the clinical point of view includes constipation, orthostatic hypotension, postprandial hypotension and implies the baroreceptor reflex.

The cardiac autonomic dysfunction may be present in the early stages of the Parkinson's disease because the ^{123}J – metaiodobenzylguanidine captation at the level of the heart is reduced in those patients, even without cardiac signs.

The neurodegenerative process in the Parkinson's disease begins from the dorsal nucleus of the vague, locus coeruleus, raphe nucleus, olfactory bulb, olfactory cortex.

Present studies showed a connexion between the olfactory and the cardiac dysfunction in the patients with early Parkinson's disease.

Several studies reported that the olfactory disorders are independent of the cognitive deficit and of the evolution stage of the disease.

Other studies showed that the olfactory dysfunction is a predictor of the cognitive decline.

The olfactory dysfunction, the sympathetic and the para-sympathetic cardiac implication occur in parallel, in Parkinson's disease.

Non-motor signs of Parkinson's disease, cardiac autonomic dysfunction and olfactory dysfunction are closely related to Parkinson's disease.

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