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First cranial pair syndrome a complement to the papez circuit pathophysiology of neurological consequences secondary to infection by SARS - COV 2 COVID 19 and the spike particle

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Rodrigo Ramos
Neurologist, CRM 6698 – SC, NEUROVIDA Clinic, Brazil

Correspondence: Rodrigo Ramos, Neurologist, CRM 6698 – SC, NEUROVIDA Clinic, Balneário Camboriú, Santa Catarina, Brazil, Email rodrigoneur@hotmail.com

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Introduction

With all the advances in medicine and science throughout the 20th century, medical education worldwide was largely based on the knowledge of the Papez Circuit (1937) in which it was determined how the conscious and unconscious system of the central nervous system works. It was possible to calculate sight, hearing and touch, but smell was not mathematical. And the entire pharmaceutical industry has been based on this thesis so that today we have the possibility of molecules that bring us the possibility of providing treatment to various pathologies such as memory deficits of greater or lesser intensity to Alzheimer's, behavioral disorders from sleep disorders, depression, anhedonia, lassitude, tiredness or psychiatric changes, diseases linked to kinesia disorders from dizziness and instability to Parkinson's. During the post-pandemic course, we noticed the symptoms of patients affected by sequelae where changes in Olfaction and Gustation are predominant in the clinical examination of these patients corresponding to the dysfunctions reported above. This observational scientific work was carried out during 3 years since the beginning of the SARS-COV 2 Covid 19 pandemic and the immunizers for Covid in patient care both at hospital and outpatient level, having as an element the evaluation of Olfaction. A reverse-engineered look at how dysfunction of the first cranial nerve pair (olfactory nerves that are nano-channels not perceptible to imaging or electroencephalographic scans) affect the human body and treatment possibilities. The sense of smell.

Anatomy, physiology and pathophysiology

SARS COV 2 - COVID 19 and the spike particle behaves like an odorant leading to hypoosmia or anosmia, but in a partial or generalized, asymmetric and random way, by its characteristic, it does not choose which olfactory fiber of the Olfactory Epithelium it will compromise (complex that includes Bowman's cells that secrete mucus and odorant uptake proteins and other functions).

The first cranial pair is responsible for Perception and not smell/odor. Olfactory Receptors (olfactory support cells and fibers) are located on the roof of the ethmoid bone next to the superior nasal turbinate. Its dysfunction is made by hypoosmia or anosmia and the dysfunction on the left is more related to memory (occasional forgetfulness until aphasia or dementia) and on the right related to kinesia (dysfunction of movements - dizziness, instability motor dysfunction to parkinsonism) and can be symmetrical or asymmetrical and random, uni or bilateral according to the involvement of olfactory fibers and their respective odor receptors, inducing a blockade of the action potential stimulus and secondary neutralization of the olf (olfactory) Gamma globulin - G olf induced by intracellular hypercalcemia by Ca release, activating Calciocalmodulin that activates Phosphodiesterase 5, in addition to the release of Calcium from the smooth endoplasmic reticulum, hyper activating Phosphodiesterase 5.

With Phosphodiesterase 5 hyperactivity, blockage of cyclic AMP formation and neutralizing pathways of the olfactory bulb will occur with consequent hypoactivation of the Intorrhinal area, piriform gyrus, amygdaloid substance and hippocampi in a uni or bilateral, asymmetric or symmetric manner, leading to an arbitrary decompensation of the Limbic System and Neuro-Endocrine-Immune System disorder (22). These are Brodmann areas 34 and 28.

The Covid Effect behaves as a persistent odor that settles in the pre-cribiform lamina (or cribiform) region, near the fibers of the Olfactory Nerves, preventing electrical impulses from developing subsequent synapses. Subsequent cyclic AMP will not occur.

Because it is the only cranial nerve that does not pass through the thalamus or have a recognized thalamic excitatory or inhibitory feedback control there may only be effected the stimuli of the ascending activating reticular formation in stimulation to the thalamus and cortex in a partial or complete way. However, without adequate synaptic activity to activate the medial lateral temporal gyrus through

the Lateral Stria and the Hypothalamus, Pituitary or Cingulate Gyrus through the Medial Stria in their anterior portions, efferent responses may be disproportionate to reality.

The consequences are in excitatory or inhibitory hypo-stimulation of cortical connections, mainly of the parietal and frontal lobes in their relations to the Conscious Systems or the Unconscious System of the Papez Circuit, improved by Maclean's Triune Brain Theory. The First Cranial Pair is a purely sensory or efferent nerve with bipolar neurons. Its major importance in brain pathophysiology has generally never been observed in clinical practice.

The neuronal epithelium next to the lamina cribrosa is the only one that constantly renews itself throughout life every 6 to 8 weeks through the basal cells under healthy conditions. But over the years the degree of cell renewal can also become slower. Something similar also occurs at the level of taste cells in the palate at the level of the tongue, but 10% of this pathway is not from the olfactory having a thalamic connection before the Amygdaloid Formation.

Smell is responsible for the perception of space and surroundings. Smell provides you with the perception of space that your Sight, Hearing and Touch suggest to you. Olfaction provides the reactive insight mainly in the part of the Papez Circuit in relation to the unconscious control system, with some relation to the frontal and parietal lobes.

The sense of smell is more focused on the odors of camphor, musk, floral, menthol, ethereal, spicy and others, but it is estimated that the human being is already programmed for around tens to hundreds of different types of olfactory perceptions. Not just smell and taste, but including behavior and reactivity.

In over 10,000 years, humans have not changed their physiology at all. But it was not possible for Dr. Papez to measure Smell in a mathematical way. In 1937 it was already possible to measure Sight, Hearing and Touch, but not Smell. After the Covid Effect, we have the opportunity to learn for the first time on a large scale about the consequences of olfactory dysfunction.

Other animals have a more or less exuberant amount of olfactory fibers in relation to visual perception, considering that the visual possibility can even be calculated, but the sensory of Olfaction is only estimated for now. For example, the Elephant smells water from miles away and for Human Beings there is a concept that healthy water has no odor. It doesn't mean that Human being doesn't have the ability to sense and perceive the Odor of healthy water.

The sense of smell is considered to perceive the odors of camphoraceous, musky, floral, mentholated, ethereal, spicy and putrid in relation to smells, but the sense of smell has never been considered as the perception of space.

As in Vision we perceive the awareness between Infrared and Ultraviolet, Smell also has its timbres. And timbres are wavelengths like Sight, Hearing, Taste and Touch.

The possibility that there is a catalytic factor by emission wavelengths, it is necessary to study it properly. Pathologies such as trauma, acquired or congenital anatomical alterations, infections, tumors, facial or craniofacial procedures were considered as causes of olfactory alterations.

The other pure sensory nerves are the Optic nerve (vision and visual fields) and Vestibulocochlear (balance and hearing) and the mixed nerves are the Trigeminal (sensitivity and motricity of mastication), Facial (facial motricity and gustation), Glossopharyngeal Nerve (swallowing and taste of the posterior third of the tongue) and Vagus Nerve (swallowing, phonation and parasympathetic activity of the chest and abdomen), but these also have their connections with the Thalamus.

The olfactory nerve originates in the telencephalon

The sense of smell begins in the olfactory epithelium located on the roof of the ethmoid bone in the lamina crivosa.

Olfactory receptors are bipolar neurons. They emit several cilia that transduce the chemical stimulus to electrical. There are on average 20 bundles of olfactory fibers bilaterally, of unmyelinated nerves, which are homolaterally destined to the ipsilateral Olfactory Bulb (on the same side, right or left and do not cross in the intra nasal part) through the Crivous Blade.

In the Olfactory Bulb are the mitral cells and the tufted cells, or M-T, in the formation of the Olfactory Tract that runs along the base of the frontal lobe in the Olfactory Sulcus to the anterior perforated formation and originates the medial and lateral olfactory striae arriving at the Olfactory Trine. On its way, the Olfactory Tract divides medially-posteriorly into the Medial Stria which joins the interhemispheric region in the anterior commissure - diencephalon and the Lateral Olfactory Stria carrying the stimulus to the Primary Olfactory Cortex, in the medial lateral temporal gyrus (Uncus, Parahippocampal Gyrus and Hippocampus) being considered the Pre-Piriformal area, Periamygdaloid Area, forming the Secondary Olfactory Cortex. The Intorinal Area. is part of the Paleocortex.

The olfactory pathway does not pass through the thalamus and is not controlled by the thalamus. The virus or Covid Effect does not enter the central nervous system, it only makes a bioelectric blockade leading to slow and progressive multiple organ failure. Upper Motor Neuron Atrophy is slow. The Covid/Spike Effect can directly induce decompensations of coagulation and inflammation because, although it depends on the Hypothalamic-Pituitary-Limbic Axis, if the olfactory stimulus does not reach the cerebral cortex correctly or is not present due to cancellation of the initial action potential, the cortex misinterprets the environment and sends an adverse efferent command to the body systems (inflammation, coagulation, autoimmune and others).

The Orbitofrontal Cortex is probably where you are aware of odors. Smells are a materialization in consciousness of a pre-existing experience. It is questioned whether there is communication with the Thalamus. There is the possibility of the Olfactory Tubercle communicating to the Dorsal Medial Nucleus of the Thalamus and from there radiating to the Orbitofrontal Cortex, or the Anterior Olfactory Nucleus or even the Intorinal area with direct communication to the Orbitofrontal Cortex, or an association between the three possibilities. The Triune Brain theory considers that the anterior nucleus of the thalamus and all the thalamic nuclei have the function of perceiving emotions, but cannot interpret, and sends the information to the cingulate gyrus where the information is already added and elements to send to the cerebral cortex for the interpretation of the stimulus. But if the hypothalamic region in the Intorinal Gyrus is not activated, there will be no adequate activation, generating dysfunctions of the Hypothalamus, Amygdala, Fornix, Cingulate Gyrus and other cortical associative areas. Paul Broca, in 1878 had already described the Limbic System.

At the end of the 18th century, Willians James described that changes in perception could cause a positive or negative situation

in relation to the stimulus. He demonstrated how a sensation and perception can give a physiological response to a given stimulus. In 1929 the Cannon Bard Theory emerged. He considered that the Thalamus as the great center of reception of sensory information (but only in relation to the information of Vision, Hearing, Gustation and Touch), and that this message is divided to the Cortex indicating Consciousness and to the Hypothalamus will generate responses to our peripheral neurovegetative systems in relation to the Autonomic Nervous System, Sympathetic and Parasympathetic.

In 1937, James Papez described the Papez Circuit, which proposes that stimuli go from the Hippocampus to the Fornix, from the Fornix to the Mamillary Bodies, from the Mamillary Bodies to the Thalamus and then to the Cingulate Gyrus, and back to the Hippocampus. Papez believed that all these stimuli were responsible for his endocrine, emotional, visceral and voluntary responses to the environment. But it turned out that it might be more related to Memory than Emotions. In 1952, Paul Maclean added to Papez's Circuit new structures such as the Septal Area, and the Amygdala, with the Amygdala being considered as the center of the Limbic System.

In 1990 Paul Maclean published the Triune Brain Theory, separating the Brain functionally into 3 parts, the Neocortex, Reptilian Complex and Limbic System. He could not consider the importance of Smell, as Smell was not measurable in a mathematical way, only random. Wernieke's Area was considered as a center of the Sensory Cortex in its relations to the Cingulate Gyrus.

We are learning about Smell in its dysfunction or loss of this sensory sense. Unconscious emotional experiences are made by information that comes from association areas that enter the Cingulate Gyrus, goes to the Hippocampus (but still has the olfactory activation of the Intorinal Gyrus), which stimulates the Cerebral Amygdala and the physiological reaction. This information returns to the Hippocampus, makes the circuit of the fornix, Mamillary Body, Mammillothalamic Tract and Anterior Nucleus of the Thalamus. From the Anterior Nucleus of the Thalamus it goes to the Cingulate Gyrus and from there, it returns to the Hippocampus and does not go to the Cerebral Cortex. This emotion does not go to the Cerebral Cortex. Unconscious emotion is triggered by subjective information that the Cerebral Cortex cannot distinguish which change is occurring and which stimulus is responsible for the physiological change.

Symptoms such as malaise, oppression, depression, memory deficits or confused thinking, instability, tiredness, lack of energy, anhedonia are related to this system. Everyone breathes unconsciously. It is the Olfactory System Perception, the sense of smell, that modulates this information. If there is a loss of activity of the Anterior Cingulate Cortex due to olfactory dysfunction, there may be a change from aggression to more domesticable behavior, but the reverse is also plausible depending on the laterality of the olfactory involvement.

It is possible to understand how the olfactory system is directly related to rapidly or slowly progressive neurodegeneration. It is already known that people diagnosed with dementia - Alzheimer's disease or Parkinson's disease - can have loss of smell many years before conclusive diagnosis. It was just not known what the etiology was. The Electrical Field in the Olfactory Substance may be affected by its pre-comorbidities or even be the cause of them. Diabetes, trauma to the ethmoid bone and adjacent areas, adenoid surgery, IgA deficiency, previous infections, use of licit or illicit drugs, social conditions associated with chronic contamination of upper airways, especially intra nasal, excessive exposure to magnetic fields, among other situations are conditions for diseases secondary to olfactory dysfunction. Possibly dysfunction of the pre amygdaloid olfactory area.

But in my opinion there has to be a wavelength pattern being the catalyst of the neurological effect, beyond the direct or indirect neurodegenerative pictures of the Olfactory System. I believe it is a determinant of the Behavior of the Human Being. This question does not interfere with the possibility of treating the specific situation. Anosmia and hypoosmia.

Therapies currently used

All therapeutic possibilities are focusing on the Virus and or what happens in the Human Being, but at the level of Olfaction and its importance to the stimulation of the Central Nervous System we have little information. We did not find any alterations in the imaging or liquid exams that would indicate a path. Scalp Electroencephalography also lacks precision in relation to the Olfactory System or the Limbic System. But in Anatomophysiology and Electroneurophysiology we can find these paths, understanding the sequelae, and by reverse engineering understand the pathophysiological process of the consequences of the alterations of Olfaction being able to better understand what Broca, Bard, Papez, Maclean realized and taught us.

Among the most frequently used alternatives we can mention:

I. Dexamethasone, Methylprednisolone and other corticosteroids can increase the volume of water in the olfactory pathways and thus dilute the mucus between the olfactory receptors affected by the Covid Effect, because the olfactory receptors are activated only by hydrophilic form. In addition, it has an anti-inflammatory action. It acts on Phosphodiesterase A2 most related to the lower airways.

II. Mabs are related to possibilities of greater difficulty of clinical hospital support in relation to most of the population, even if offered by state institutions. And they are not necessarily physiological, but can be more interventionist like vaccines that act on mRNA. They are an excellent possibility and many studies are underway

III. Immunizers for Covid 19 and its mutations are very questionable, as they were not really effective in controlling the Pandemic and in the package insert the risk and side effects such as thrombosis and myocarditis are already reported.

IV. Hydroxychloroquine acts on the glycolization of Angiotensin Converting Enzyme ACE - 2 and, can also act on the inhibition of phosphodiesterase 5 of the olfactory epithelium, and, with this control or even reverse apoptosis in a coagulative way by intracellular hypercalcemia that leads to the owners of the olfactory epithelium and its systemic consequences. There are other phosphodiesterase 5 blockers, but with other side effects more difficult to human behavior. Sildenafil is one of them, but except for application in female patients and without its contraindications, it does not seem to me the most suitable form for early treatment or even post-Covid. Although it also has ACE-2 expression there may be more venous congestion or behavioral changes for males; which I do not think is recommended for minor situations, but in ICU or pre ICU it could be evaluated very carefully. This medication has already been proposed in cystic fibrosis of the lungs, but in already sequelae cases it was not so promising.

V. Iverrmectin promotes specific inhibition of Importin-α/β-mediated nuclear import. Thus, it impacts the nuclear transport of viral proteins dependent on this protein, resulting in the suppression of replication of several RNA viruses, including HIV, chikungunya virus and yellow fever virus.

VI. The use of arginine and phosphatidylserine seem to be promising possibilities in the reconstitution of the olfactory substance.

VII. The application of tDCS or tDCS Neuromodulation has the potential to reverse the hyperpolarized electric field in the extracellular of the intra nasal region of the ethmoid bone the Olfactory Nerves before entering the Crivosa Plate, in order to electrically stabilize the ionic fields in the Olfactory System until their references in the Limbic System and Orbital Fronto. Neuro Modulation Brain tDCS or tDCS already has level 1-A Evidence in Depression, and with minimal risk of side effects being applied by trained Professional. In addition to publications in relation to sequelae of lesions of the Occipital Lobe, Motor Areas and other situations of neurological diseases.

VIII. The role of the Transmembrane Serine Protease TMPRSS2 should also be observed. In recent publications in the northern region of Brazil, Proxaglutamine was effective in counteracting this TMPRSS2 protein.[1–17]

General considerations

The Theory of Magnetism or something similar to magnetism, like Whales or Dolphins stranded on the beach due to loss of Perception, may have to teach us about our Olfactory System. The virus does not infect the intracranial brain because the brain begins in the first cranial pairs in the intra nasal Olfactory Substance, in the upper third of the upper nasal cavities at the bottom of the Ethmoid bone. The First Cranial Pair, the Olfactory Nerves average 20 cranial pairs where life and living begins. The Covid Effect is randomized and asymmetrical dysfunction of the olfactory nerves, but mild to severe hypo-attenuation of the olfactory bulb. It is an electrical dysfunction that secondarily involves The Cycle of Papez (1937) and The Limbic System of Paul D. Maclean (1952) and the same Paul Maclean the Triune Brain (1990). A possible addition to these theories was that the prefrontal cortex was considered to be tertiary. It considered Vision as primary. Olfaction is the first to provide stimulation to the amygdalae, and hypo-stimulation is interpreted as depression, fear, lack of attention, lack of attitude or alertness symptoms, lack of dynamics/kinesis, but without direct thalamic control there are no effective feedback circuits, and only the ascending reticular formation does its best for minimal survival.

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None.

Conflicts of interest

The author declares there is no conflict of interest.

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