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Supplementary File

Abulia Major and Hypoactive Delirium in COVID-19 Reversed with Methylprednisolone Pulse Therapy

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APPENDIX

Syllabus

Table 1: Thesis of the article.

FIGURES FOR ASSESSMENT OF GRADE OF DEPENDENCY

Table 2: Katz Index Classification, according to the level of dependence in bathing, dressing, toileting, transferring, continence, and eating.

Patient Name:_____ **Date:**_____
Patient ID #_____

Katz Index of Independence in Activities of Daily Living

Activities Points (1 or 0)	Independence (1 Point) **NO** supervision, direction or personal assistance.	Dependence (0 Points) **WITH** supervision, direction, personal assistance or total care.
BATHING Points: _____	**(1 POINT)** Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity.	**(0 POINTS)** Need help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing
DRESSING Points: _____	**(1 POINT)** Get clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	**(0 POINTS)** Needs help with dressing self or needs to be completely dressed.
TOILETING Points: _____	**(1 POINT)** Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.	**(0 POINTS)** Needs help transferring to the toilet, cleaning self or uses bedpan or commode.
TRANSFERRING Points: _____	**(1 POINT)** Moves in and out of bed or chair unassisted. Mechanical transfer aids are acceptable	**(0 POINTS)** Needs help in moving from bed to chair or requires a complete transfer.
CONTINENCE Points: _____	**(1 POINT)** Exercises complete self control over urination and defecation.	**(0 POINTS)** Is partially or totally incontinent of bowel or bladder
FEEDING Points: _____	**(1 POINT)** Gets food from plate into mouth without help. Preparation of food may be done by another person.	**(0 POINTS)** Needs partial or total help with feeding or requires parenteral feeding.

TOTAL POINTS: _____ **SCORING:** 6 = High (*patient independent*) 0 = Low (*patient very dependent*

Source: Hartford Institute for Geriatric Nursing. Home | Hartford Institute for Geriatric Nursing (hign.org). Accessed on 23/05/2022.

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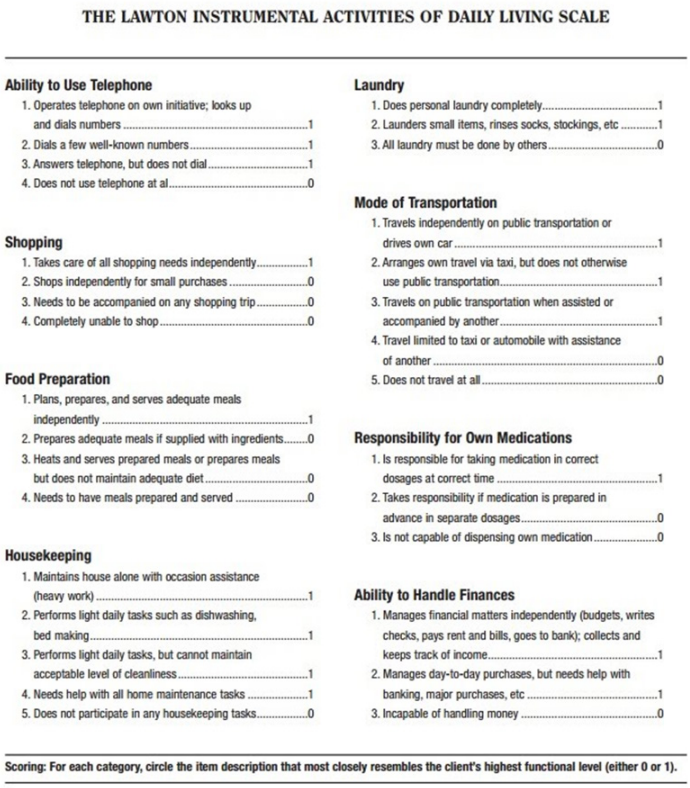
Table 3: Lawton Instrumental Activities of Daily Living (IADL).



THE LAWTON INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE

Ability to Use Telephone
1. Operates telephone on own initiative; looks up and dials numbers 1
2. Dials a few well-known numbers 1
3. Answers telephone, but does not dial 1
4. Does not use telephone at al 0

Shopping
1. Takes care of all shopping needs independently 1
2. Shops independently for small purchases 0
3. Needs to be accompanied on any shopping trip 0
4. Completely unable to shop 0

Food Preparation
1. Plans, prepares, and serves adequate meals independently 1
2. Prepares adequate meals if supplied with ingredients 0
3. Heats and serves prepared meals or prepares meals but does not maintain adequate diet 0
4. Needs to have meals prepared and served 0

Housekeeping
1. Maintains house alone with occasion assistance (heavy work) 1
2. Performs light daily tasks such as dishwashing, bed making 1
3. Performs light daily tasks, but cannot maintain acceptable level of cleanliness 1
4. Needs help with all home maintenance tasks 1
5. Does not participate in any housekeeping tasks 0

Laundry
1. Does personal laundry completely 1
2. Launders small items, rinses socks, stockings, etc 1
3. All laundry must be done by others 0

Mode of Transportation
1. Travels independently on public transportation or drives own car 1
2. Arranges own travel via taxi, but does not otherwise use public transportation 1
3. Travels on public transportation when assisted or accompanied by another 1
4. Travel limited to taxi or automobile with assistance of another 0
5. Does not travel at all 0

Responsibility for Own Medications
1. Is responsible for taking medication in correct dosages at correct time 1
2. Takes responsibility if medication is prepared in advance in separate dosages 0
3. Is not capable of dispensing own medication 0

Ability to Handle Finances
1. Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income 1
2. Manages day-to-day purchases, but needs help with banking, major purchases, etc 1
3. Incapable of handling money 0

Scoring: For each category, circle the item description that most closely resembles the client's highest functional level (either 0 or 1).

Source: Adapted from LAWTON dez 2015.pdf (usp.br). Accessed in 23/05/2022.

DETAILS ABOUT PATIENT EXAMS

Case 1

The referred patient has a diagnosis of notable mucosal oedema in the sinuses, showing that there was something inflammatory in the high airways compatible with SARS-CoV-2 viral replication sites (image not available). In addition, the hyper signal changes in the brain parenchyma are compatible with the main findings provoked by COVID-19.

Laboratory tests have the following points to be highlighted: leukocytosis, the elevation of reactive C protein, dyslipidaemia without the existence of previously reported metabolic disorders, and ferritin over the limit value. These changes may be related to the characteristic metabolic deviation caused by SARS-CoV-2 (Warburg effect).

Cerebrospinal fluid was normal. Tests not available that could help in the diagnostic investigation of relationship in serum of Tryptophan/Kynurenine concentrations. Autoimmunity tests performed: anti-dsDNA, anti-RNP, anti-Smith (or anti-Sm), anti-Sjogren's SSA and SSB, anti-scleroderma or anti-Scl-70, anti-Jo-1, and anti-CCP: all of them were negative.

Table 4: Case 1 exams.

Exams	Results	Reference value
	Biochemistry	
Creatinine (01/05/2021)	Result: 0.85 mg/dL	1,2 mg/dL
Urea	Result: 32 mg/dL	49 mg/dL
	Urine	
Chemical Physical Examination	Colour: Citrus Yellow Appearance: Slightly turbid Density: 1,025	Light Yellow, Citrus, Clear/Lig. Turbid 1005 to 1030
pH reaction	6,5	5.5 to 7.0
Proteins (mg/dL)	Absent	Up to 10 mg/dL
Reducing substances	Absent	Absent
Ketones	CLUE	Absent
Bilirubins	Absent	Absent
Haemoglobin	Present	+Missing
Urobilinogen (umoL/L)	16,0	Up to 16 umol/L
Nitrite	Negative	Negative
	Analysis of figured elements	
Leukocytes	13	Up to 10,000/mL
Erythrocytes	6	Up to 5,000/mL
Epithelial Cells	Rare	Absent/Rare
Bacterial Flora	Discreet	Absent/Discrete
Haemogram		
Red blood cells (millions/mm3) Hemoglobin (g/dL)	4,72	4.32 to 5.66 million/ mm3
Hematocrit (%)	14,2	13.3 to 16.7 g/dL
	42,3	39.0 to 50.0%
	Leukogram	
Leukocytes (/mm3) Counted Cells	6.721 100% per mm3	3,700 to 11,000/mm3
Eosinophil Neutrophils	1,0	67 0 to 300/mm3
Basophils	57.0-3,831	1,700 to 7,500/mm3
Eosinophils	0.0 0	0 to 460/mm3
Lymphocytes	2.0-134	0 to 130/mm3
Monocytes	33.0-2,218	1,000 to 4,200/mm3
Platelet	7.0-470	200 to 600/mm3
	224,600/mm3	150,000 to 450,000/ mm3
	Haemogram (18/05/2021)	
Erythrocytes	4,750,000/mm3	
Hemoglobin	14.2 g/dl	

Haematocrit	42.30%	
Leukocytes-Global	15,500/mm3	
Neutrophils Rods	2.0%;310/mm3	
Segmented Neutrophils	78.0%;12,090/mm3	
Lymphocytes	13.0%;2,015/mm3	
Atypical lymphocytes	0.0% ;0/mm3	
Monocytes	6.0%;930/mm3	
Eosinophils	1.0% 1;55/mm3	
Basofylos	0.0% 0/mm3	
Metamyelocytes	0.0% 0/mm3	
Myelocytes	0.0% 0/mm3	
Promyelocytes	0.0% 0/mm3	
Blasts	0.0% 0/mm3	
Atypical Cells	0.0% 0/mm3	
Platelets	237,000/mm3	
NOTE: ANISOCYTOSIs(+)		
	Biochemistry	
FERRITIN	547.8 ng/mL	REFERENCE VALUES: WOMEN: 11.0 A 306.8 ng/mL, MEN: 23.9 A 336.2 ng/mL
ULTRA SENSITIVE PCR	1.0 mg/L	LESS THAN 10.0 mg/L
UREA	45.8 mg/dL	19.0 to 49.0 mg/dL
CREATININE 0.86 mg/dL		
TGO/AST	10U/L	REFERENCE VALUES: MEN: LESS THAN OR EQUAL TO 40.0 U/L, WOMEN: LESS THAN OR EQUAL TO 33.0 U/L
TGP/ALT	34U/L	
	CSF routine (19/05/2021)	
Colour	Colourless	Colourless
Aspect	Clear	Clear
Leukocytes for m3, Red blood cells w/mm3	0, 45	0 to 5 cells/mm3 Missing
Leukocyte differential	Note: Differential count was not performed due to an insufficient number of cells.	
	Biochemical analysis	
Total Proteins Method: Colorimetric - Automated	49 mg/dL	15 to 45 mg/dL
Glucose, Method: Colorimetric - Automated	55 mg/dL	> 60 mg/dL
Chlorine, Method: Potentiometric	120 mEq/L	120 to 130 mEq/L
LDH, Method: Multiple point kinetics	48 mg/dL	+/- 10% of the serum value
Lactic Acid - Lactate Method: Colorimetric - Automated	1.5 mmol/L	1.2 to 2.1 mmol/L
	Microbiological analysis	
Bacterioscopy Method: Microscopy - GRAM Staining	microorganisms were not visualized by Gram Method.	Absence
Fungus research, Method: China Dye	No fungic structures were visualized in the sample examined.	No fungi structures were visualized in the sample examined
	CSF ROUTINE (01/05/2021)	
Macroscopic Analysis		Reference values
Colour	Colourless	Colourless
Aspect	Clear	Clear
Leukocytes for m3, Red blood cells w/mm3	1,30	0 to 5 cells/mm3 Missing
Leukocyte differential	Note: Differential count was not performed due to an insufficient number of cells.	
	Biochemical analysis	
Total proteins. Method: Colorimetric - Automated	32 mg/dL	15 to 45 mg/dL
Glucose, Method: Colorimetric - Automated	69 mg/dL	> 60 mg/dL

Chlorine, Method: Potentiometric	125 mEq/L	120 to 130 mEq/L
LDH, Method: Multiple point kinetics	48 mg/dL	+/- 10% of the serum value
Lactic Acid - Lactate Method: Colorimetric - Automated	1.6 mmol/L	1.2 to 2.1 mmol/L
Microbiological analysis		
Bacterioscopy Method: Microscopy - Gram Staining	Microorganisms were not visualized by the Gram method.	Absence
Fungus research Method: China Dye	No fungi structures were visualized in the sample examined.	No fungi structures were visualized in the sample examined

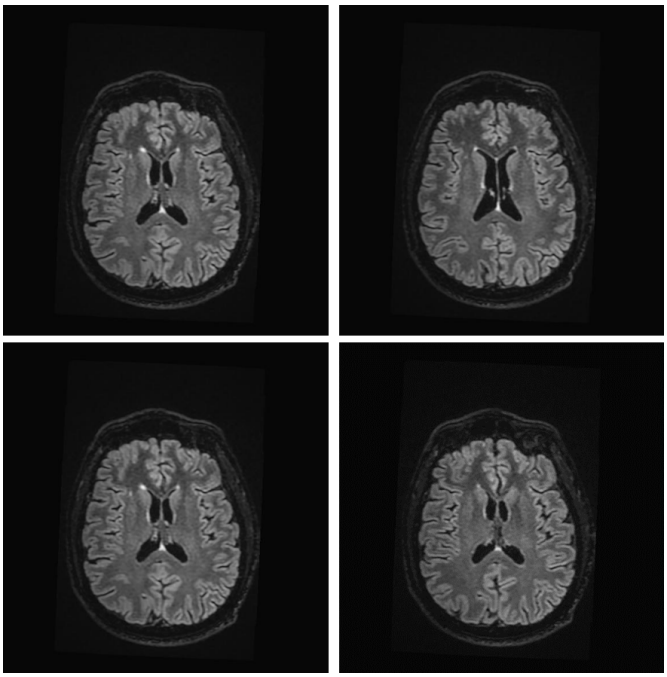


Figure 1: Magnetic resonance encephalography. Technique: Sagittal T1, axial T2, axial FLAIR, axial diffusion, axial SWAN and coronal T2. Report: There is no evidence of an intraparenchymal expansive process, extra-axial fluid collections, hypertensive ventriculomegaly, deviation of midline structures, effacement of base or focal areas of haemorrhage above or below the tentorium. There are no acute/subacute ischemic lesions detectable on the Echo-Planar sequence. The corpus callosum is well-formed, with an anatomical appearance. The ventricular system has normal topography, morphology and dimensions. The anatomical aspect of the basal cisterns and the convexity of the cerebral hemispheres. Rare small, circumscribed foci of T2/FLAIR hyper signal in supratentorial white matter periventricular and semioval centres, which do not determine a significant expansive effect or restriction to water diffusion, nonspecific, but which may represent foci of gliosis and/or myelin rarefaction. The normal signal strength of the rest of the white and grey matter in the brain. There were no signs of hippocampal sclerosis or hypothalamic lesions. Habitual flow at the level of the great arteries of the vertebrobasilar and carotid systems, according to the spin–echo criterion. Normal transparency of the visualized portions of the sinuses.

Output: Rare small, circumscribed foci of T2/FLAIR hyper signal in white matter periventricular supratentorial and semioval centres, nonspecific, but which can be foci of gliosis and/or myelin thinning.

Case II

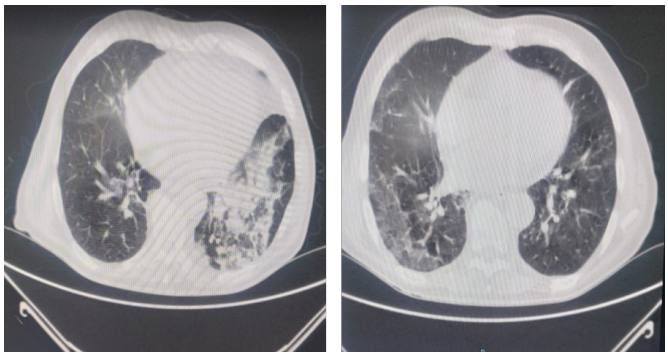


Figure 2: Chest CT scan showing ground-glass attenuation in the left lung, compatible with COVID-19. At hospital admission, the patient had a C-reactive protein of 20 mg/L, with a limit of 0.5 mg/L. After 5 days of hospitalization, he was discharged with a C-reactive protein of 3.0 mg/L.

PATHOPHYSIOLOGY

Dopaminergic and Serotoninergic changes in COVID-19: The common central mass of white matter with an oval appearance in horizontal sections of the brain is termed the centrum semiovale. It is found above the lateral ventricles and is formed by the superior longitudinal fasciculus, corona radiata, cingulum, and callosal fibres. Observational series have reported the presence of CNS symptoms in 31%6 to 69%2 of patients with severe COVID-19 vs 21% in patients with no severe COVID-19 (severity being established according to respiratory status). Dizziness (17%), headache (13%), impaired level of consciousness (8%), acute stroke (3%), ataxia (<1.0%), and seizures (<1.0%) were the main symptoms or syndromes reported in hospitalized patients.6 Agitation (69%), confusion (65%), signs of corticospinal tract dysfunction (67%), and impairment of executive functions (36%) were frequent symptoms in an observational series of 64 consecutive patients admitted to 2 intensive care units (ICUs) due to acute respiratory distress syndrome caused by COVID-19 [1,2].

The most frequent neuroimaging findings described were signal abnormalities located in the medial temporal lobe in 43% of patients; no confluent multifocal white matter hyper intense lesions on FLAIR and diffusion, with variable enhancement and associated with haemorrhagic lesions in 30% of patients; and extensive and isolated white matter micro haemorrhages were detected in 24% of patients. Few cases of transverse myelitis associated with COVID-19 have also been reported [3].

The disorders related to changes in dopamine and serotonin in COVID-19 are explained by inflammation in the central nervous system and by the low absorption of its substrates phenylalanine (dopamine and catechol amines) and tryptophan (serotonin, kynurenine, vitamin B, and NAD/NADH+). It is common for critically ill patients to present hyperthermia, and this fact occurs due to the imbalance of these neurotransmitters.

The GABAergic inhibitory output from the brain thermostat in the preoptic area POA to the temperature control subaltern neural

circuits (Raphe Dorsalis Nucleus and Raphe Pallidus Nucleus) is a function of the balance between the receptor-mediated (opposite) effects of transient receptor potential TRPM2 and EP3 prostaglandin receptors. Activation of neurons that express TRPM2 in the POA favours hypothermia, while inhibition has the opposite effect. However, EP3 receptors induce an increase in body temperature. Activation of neurons expressing EP3 in the POA results in hyperthermia, while inhibition has the opposite effect. TRPM2 agonists and/or EP3 antagonists may be beneficial in controlling hyperthermia.

In addition, quinpirole-mediated inhibition of Brown Adipose Tissue (BAT) thermogenesis was blocked by pre-treatment with dopamine D2 receptor antagonists that cross the blood-brain barrier but not by domperidone, a peripherally acting dopamine D2 receptor antagonist. By directly recording BAT sympathetic nerve activity in anesthetized rats, we confirmed that quinpyrole reduces sympathetic outflow to BAT.

Dopamine participates in a person's movement, coordination, and feelings of pleasure and reward. Serotonin is also involved in emotions, but it also affects digestion and metabolism.

Abulia, also known as apathy, psychic akinesia, and athymia, refers to the lack of will, impulse, or initiative for action, speech, and thought and appears to be related to dysfunctions in the brain's dopamine-dependent circuits. Abulia can be conceptually like lying on a continuum of motivational and emotional deficit in which apathy is at one extreme and kinetic mutism at the other, more severe extreme.

Conditions causing damage to the basal forebrain: Trauma, anterior cerebral artery territory infarction and ruptured anterior communicating artery aneurysms, blunt traumatic brain injury Parkinson's disease, other causes of frontal lobe disease: tumour, abscess, frontal lobotomy, metabolic and electrolyte disturbances: hypoxia, hypoglycaemia, hepatic encephalopathy.

Abulia Minor (Apathy): Patients with minor abulia may respond to requests from others and take part in activities that others start but do not initiate plans or activities of their own. Pleasure and motivation, whether they are present. They may say little spontaneously but give brief responses when others speak to them. Some patients may “talk a good game”, telling others about some plans, but never carry them out. Initiation is dissociated from volition [4,5].

Abulia Major (Akinetic Mutism): The patient will not start anything at all, including talking and eating, and may require full personal care. Akinetic mutism is a state of limited verbal and motor response to the environment in people without paralysis and coma. Patients may have open eyes and brief movements. In lesions involving the anteromedial lobes, speech and agitation to unpleasant stimuli may occur. The eyes of these patients are open and follow objects, and they are more alert than those with midbrain or thalamic lesions. Patients can also give a brief, monosyllabic, but appropriate response to questions.

"Miller Fisher Phone Effect"-Patients with abulia can sometimes talk at length fluently and animatedly on the phone.

Thus, it is important to prove that since the dopaminergic and serotonergic pathways are suppressed by SARS-CoV-2 infection, drugs that inhibit these pathways should not be used, as they will delay the patient's improvement, for example, prolonging the intubation time. Due to extubating failure related to muscle control and the patient's drowsiness state.

Treatment for abulia is dopamine replacement; in addition, studies show that patients using serotonin reuptake inhibitors had a better outcome than those who did not use this class of drugs [6,7]. COVID-19 is a challenge that has been imposed on us. Recognizing our limitations is the first step toward finding solutions in the face of so many doubts [8,9].

PATHWAYS

1- Kynurenine toxic products and tryptophan deficiency due to the internalization of ACE-2 in the intestine.

Tryptophan (Try) is metabolized, when in homeostasis, by the liver enzyme TDO. Upon inflammatory processes, which play the role of tryptophan metabolism, IDO-1 is produced by dendritic cells and monocytes, with IFN-gamma as the main stimulus. Try metabolism, when performed through the inflammatory environment, tends to divert from normal via kynurenine by-products, most of which are toxic to the Central Nervous System (CNS). The pathways of Try metabolism are the serotonin/melatonin pathway and the vitamin B3 pathway (NAD/NADH+). Gastrointestinal symptoms of COVID-19 may show great internalization of ACE-2, which is also responsible for the absorption of tryptophane and phenylalanine. Thus, acute depressive conditions and changes in mood and behaviour have been very present in COVID-19 patients. The lack of phenylalanine absorption leads to a deficiency in the dopaminergic pathway [10].

Adenosine pathway

Adenosine is produced from metabolic and hypoxemic stress in response to cell damage. In COVID-19, the patient has severe hypoxia due to lung injury due to the lack of NAD/NADH+ due to vitamin B3 deficiency and has its energy source diverted to oxidative stress and insulin resistance. In response, there is a large production of adenosine, whose action on CNS receptors promotes peripheral pain-like symptoms, akathisia-like agitation, anxiety or fatigue, and sleep [11].

Development of autoimmune meningoencephalitis

Viral diseases can lead to the development of antibodies that can mimic or even cause autoimmune diseases after infection. In COVID-19, cases of lupus-like syndrome have been observed, as well as immune-mediated thrombosis and other reactions resulting from viral infection. COVID-19 promotes great stimulation for neutrophils-it is a characteristic of patients to have neutrophilia approximately 8 days after the onset of symptoms. Neutrophils evolve in NETosis, one of the bases for the formation of autoantibodies, in addition to the low production of antibodies, which is prevalent, forming immunocomplexes instead of having enough neutralizing antibodies. Autoantibodies can act on the central nervous system at NMDA2F receptors and cause meningoencephalitis [12-14].

Lymphopenia and immunosuppression

COVID-19 is marked by severe immunosuppression in patients with predictors of severity. The marked lymphopenia stimulated both by viral action and by the time of exposure to a hypoxic environment can lead to reactivation of latent infectious diseases, for example, reactivation of fungal and bacterial infection, and virus infections such as the Herpes viridae family (herpes virus of

different subtypes, varicella-zoster, cytomegalovirus), which can be causes of meningoencephalitis secondary to COVID-19.

Neuropsychiatric conditions in COVID-19 are related to a) inflammatory pathways, either by viral action or hypoxia, resulting in autoantibody production; b) toxic products that will act in the CNS and trigger a plethora of polymorphic signs and symptoms varying from person to person; and c) SARS-CoV-2 direct action on the CNS. However, the basis for these changes is inflammation [15,16].

Traditionally, meningoencephalitis is treated with corticosteroid pulse; in cases of refractoriness, immunoglobulin and plasmapheresis can be used.

Despite more controversies that exist about the use of methylprednisolone and corticosteroids in general, it has been the solution for COVID-19. When used properly and at the right time, the progression of the disease can be blocked. The best time in acute illness is between the sixth and eighth days of symptom onset, before the cytokine storm. In chronic conditions, there is no best time, and there is a time when the physician decides to use corticosteroids as a basis to act against inflammation.

Corticosteroids have side effects, but they are medicines that have been used for many years; as they are nonspecific, they act in several ways at the same time, and in the face of an inflammatory disease due to SARS-COV-2 infection, the nonspecific target of steroids has been our best treatment [17,18].

The NMDA receptor is a glutamate-activated calcium ionophore derived from a series of pore-forming and auxiliary subunits (Glu1, Glu2A through 2D, and Glu3A and 3B receptors) that figure out the functional properties of the native NMDA receptors. Glutamate is the primary excitatory neurotransmitter in the brain, acting at ionotropic and metabotropic glutamate receptors. Ionotropic Glutamate Receptors (iGluRs), responsible for fast neuronal communication at excitatory synapses, include three subfamilies: -amino-3-hydroxy-5-methyl-4-isoxasolepropionic acid (AMPA) receptors, kainate receptors, and NMDARs. excessive NMDAR activity causes excitotoxicity and promotes cell death, underlying a potential mechanism of neurodegeneration occurred in AD. The major factors that affect NMDAR signalling in AD include glutamate availability and the modulation of NMDAR channel functions.

Kynurenine pathway

Dopaminergic and Serotoninergic pathways

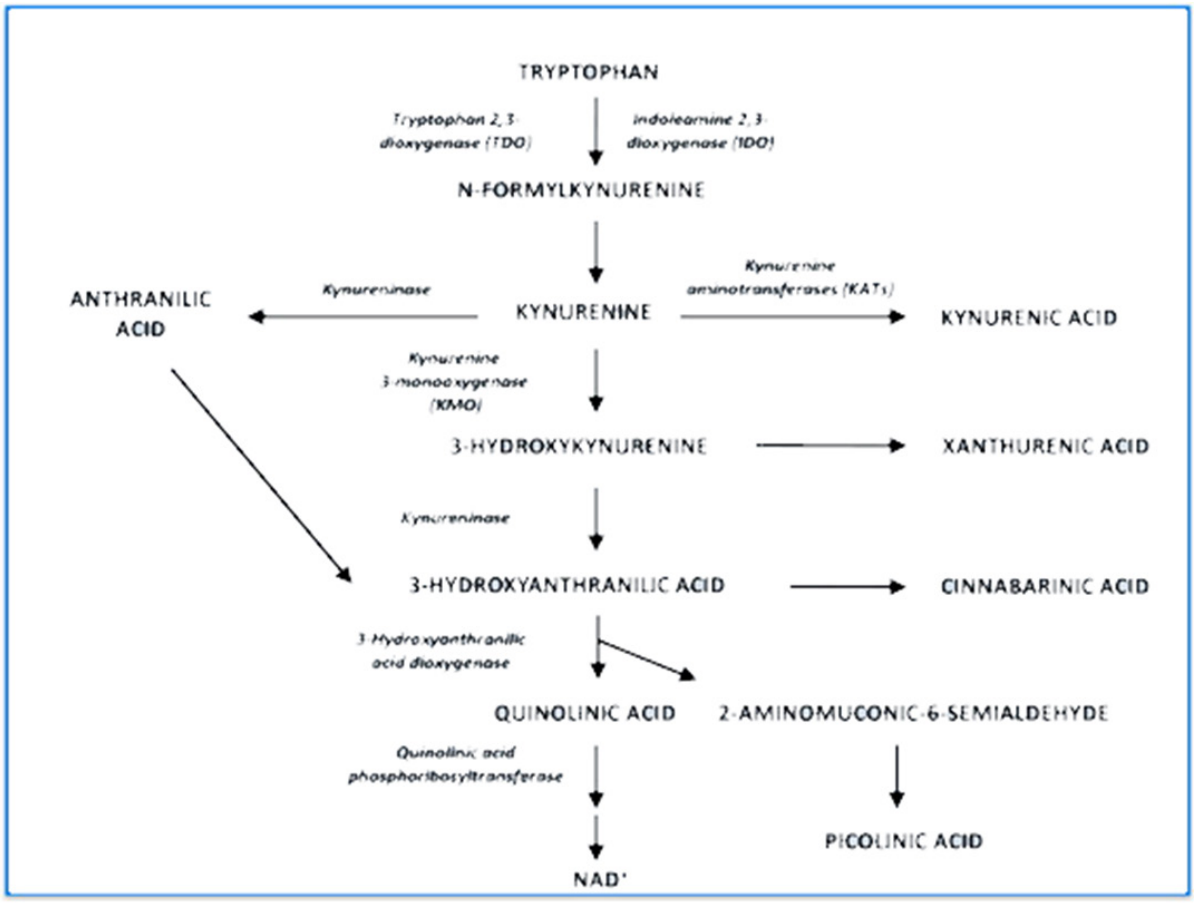


Figure 3: The Kynurenine Pathway (KP) is the major route for Tryptophan (TRP) metabolism in most mammalian tissues. The KP metabolizes TRP into a number of neuroactive metabolites, such as Kynurenine (KYN), Kynurenic Acid (KYNA), and 3-Hydroxykynurenine (3-HK), and Quinolinic Acid (QUIN). Elevated metabolite concentrations in the central nervous system are associated with the pathophysiology of several inflammation-related neuropsychiatric diseases. During an inflammatory response, the first KP metabolic step is primarily regulated by Indoleamine 2,3-Dioxygenase 1 (IDO1), which produces KYN from TRP. Following this initial step, the KP has 2 distinct branches; one branch is regulated by Kynurenine 3-Monooxygenase (KMO) and is primarily responsible for 3-HK and QUIN production, and the other branch is regulated by Kynurenine Aminotransferase (KAT), which produces KYNA, an N-methyl-D-aspartate receptor, and alpha-7-nicotinic acetylcholine receptor antagonist.

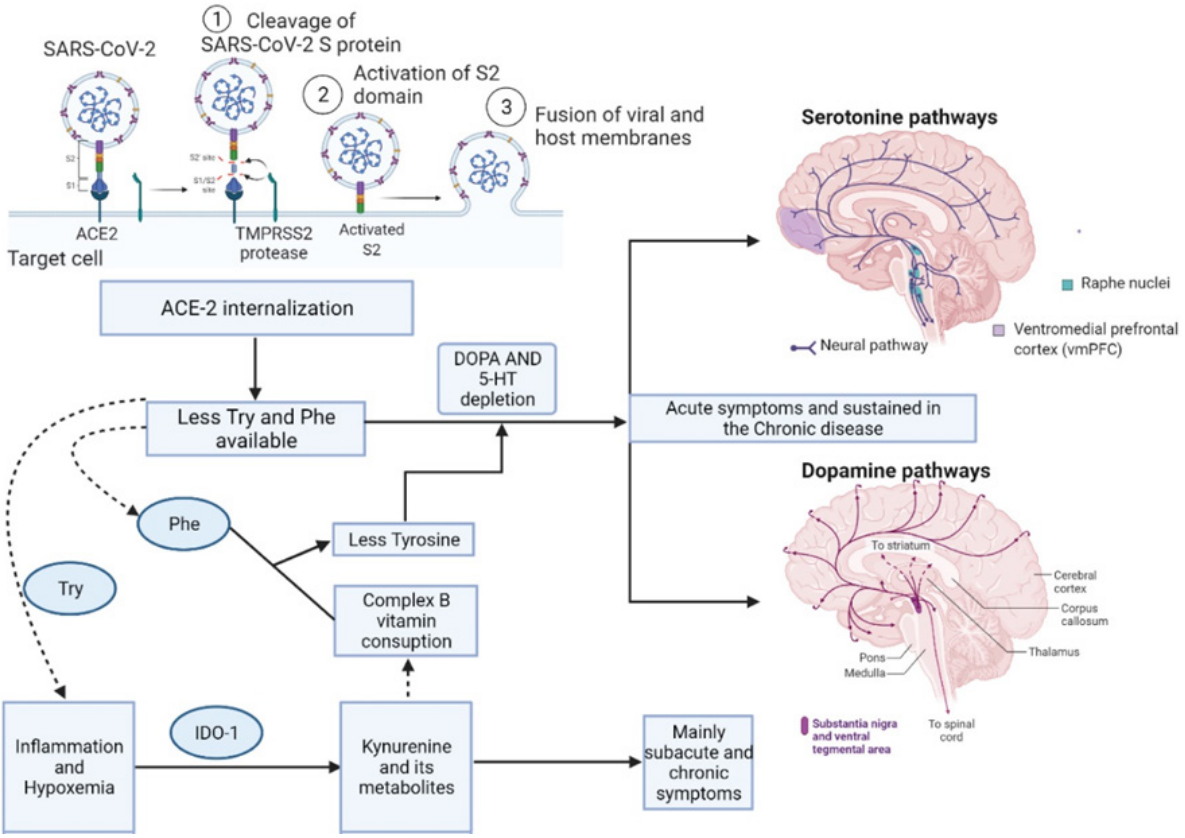


Figure 4: Changes in tryptophan and phenylalanine metabolism due to ACE-2 protein internalization in enterocytes: SARS-CoV-2 infection is systemic, causing many changes in the human body. One of these changes is the decreased absorption of some ACE-2-dependent amino acids. The acute depletion of tryptophan and phenylalanine causes acute psychiatric symptoms frequently observed in patients: mood disorders, generalized anxiety, and insomnia. These symptoms are due to the sudden decrease in 5-HT and Dopamine in the central nervous system and the peripheral intestinal serotonin produced by the enterochromaffin cells, causing many metabolic and systemic changes. Lasting hypoxemia blocks many metabolic pathways, for example, the conversion of Try to Niacin (Vitamin B3=NAD/NADH+). With the metabolism of Try performed by IDO1, there will be more formation of Kynurenine and its metabolites due to the inflammatory status. In the Central Nervous System, these metabolites can simulate rapidly progressive dementia, Alzheimer's and Parkinson's like symptoms, schizophrenia, somnolence and difficulty in sedation due to these metabolites, GABA and Glutamine receptors are saturated. These metabolites usually use B-complex vitamins as cofactors, promoting depletion of these substances, and interfering in the conversion of Phe to tyrosine. Phe: Phenylalanine; Try: Tryptophan; 5-HT Serotonin; IDO1 indoleamine 2,3-dioxygenase 1.

DISCUSSION

The two presented cases are in acute situations in patients who were previously healthy and independent or partially dependent to perform daily activities. We are facing a new virus with singularities that are still obstacles that prevent the realization of adequate therapy. It is essential to highlight that medical action must always be based on the ethics that govern the medical profession, on not harming, on offering comfort when there is no possibility of cure-always judging each situation properly and considering that the patient has a family that needs support.

The use of corticosteroids, although controversial, has gained increasing evidence in the treatment of COVID-19, with benefits when used in time and in high doses. Corticosteroids are historically used to treat viral or autoimmune meningoencephalitis and the cases presented are examples of good use of this class of medicines, resulting in patients' improvement of symptoms with a return to the health status (or near to the basal status) they had before of the illness.

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