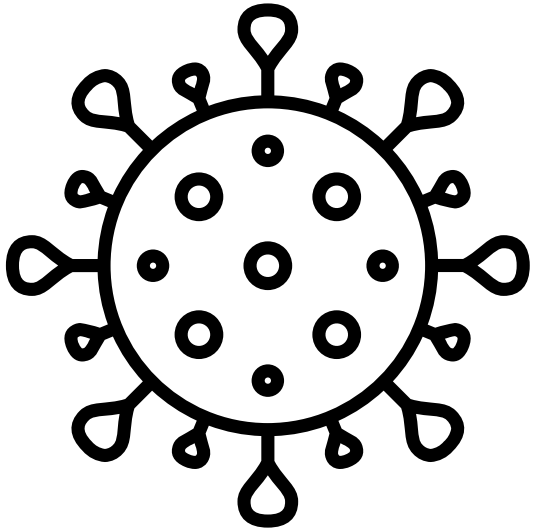
Visual Sequelae of Long Covid

A CASE REPORT AND DISCUSSION



AMANDA ZELLER MANLEY, OD, FCOVD

KRASKIN INVITATIONAL SKEFFINGTON SYMPOSIUM 2022

E.P., 36-year-old White Male

Sickened with Covid-19 in March 2020

Presented to clinic April 2021

Complaints of eyestrain with reading paper or screen, blurred vision, and afterimages. “Things look like they’re in focus but vibrating slightly.” Unless he “avoids everything” he is likely to develop a migraine. Experiences daily headache.

Current Medications and Supplements

- Sumatriptan- approximately once per week
- Vitamin D- daily
- Vitamin B12- daily
- Magnesium- daily

Ocular and other medical history

Myopia, reported no change in Rx for 8-10 years

Occasional headaches, but no history of migraine prior to encephalitis

Mild concussion at age 30; reported “migraine-like” feeling for a few days. Concussion as a child, details unclear.

No remarkable family history

Confounding Factors and Timeline

September 2019	Viral meningitis and encephalitis of unknown etiology; spent a week in the ICU. MRI unremarkable.
November 2019	Returned to work as an attorney; newly plagued by complex migraines but otherwise able to work full time. Considered recovered by his neurologist.
March 2020	Contracts Covid-19; symptoms of shortness of breath and digestive issues last 6+ months. Returns to work after a few weeks.

Confounding Factors and Timeline

January 2021

Develops neurological symptoms: brain fog, crippling fatigue, poor sleep, eyestrain, blurred vision, poor recovery from reading or other stimuli, “migraine tailspin”, “brain shakes”.

Symptoms have become so severe he can no longer work. Can read at most 5 minutes per sitting, one hour total per day. Migraine “hangover” sometimes takes 5+ days to clear. Additional migraine symptoms include numbness, tingling, muscle weakness, confusion, unsteadiness, nausea, vomiting.

Neuro-ophthalmology diagnoses complex migraine.

Confounding Factors and Timeline

February 2021	Neuro-ophthalmologist diagnoses convergence insufficiency, recommends seeing an optometrist to update glasses Rx and possibly add Fresnel prism. Suggested FL41 tint on glasses.
April 2021	Repeat MRI unremarkable. Neuro-ophthalmologist confirms convergence insufficiency, notes no nystagmus, suggests oscillopsia is secondary to vestibular migraine.

Examination Findings

Habitual Rx:

OD: -3.25 sph	20/20 distance and near
OS: -3.00 sph	20/20 distance and near

Manifest Refraction:

OD: -3.25 sph	20/20
OS: -3.00 -0.25 x 090	20/20

Examination Findings

Convergence Near Point: 12”

Unstable fixation OS

EOMs: FROM, Saccadic Intrusions during pursuits, OD better

Saccades: horizontal- acceptable, OD better; vertical- less accurate, OD better

Stereopsis: 100 seconds

Pupils equal, 3mm, slight alpha omega

Maddox Rod: 11 Δ Base In, 0.5 Δ Base Down OS

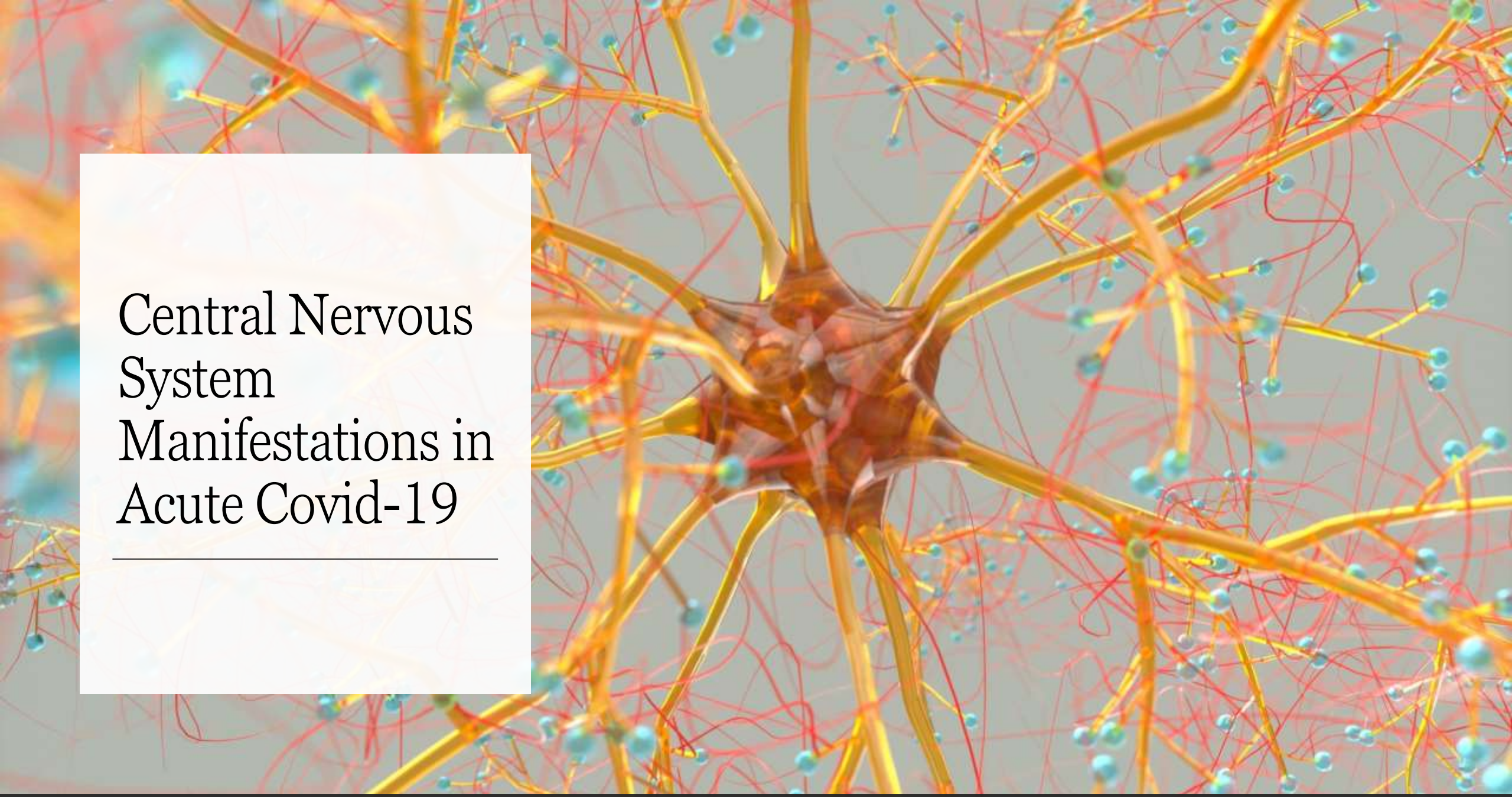
Examination Findings

Egocentric localization intact horizontal and vertical

Sensitivity to OKN drum rated 2/5 in all quadrants

Symptoms were not exacerbated by shifting weight, bending, head extension/flexion

Symptoms were not exacerbated by shifting perception between central and peripheral vision



Central Nervous System Manifestations in Acute Covid-19

Central Nervous System Manifestations in Acute Covid-19

Headaches

Impaired consciousness

Delirium

Loss of smell and taste

Encephalitis

Seizures

Strokes

Myelitis

Acute disseminated encephalomyelitis

Neurogenic respiratory failure

Encephalopathy

Silent hypoxemia

Generalized myoclonus

Neuroleptic malignant syndrome

Kawasaki syndrome

Divani AA, Andalib S, Biller J, Di Napoli M, Moghimi N, Rubinos CA, Nobleza CO, Sylaja PN, Toledano M, Lattanzi S, McCullough LD, Cruz-Flores S, Torbey M, Azarpazhooh MR. **Central Nervous System Manifestations Associated with COVID-19**. Curr Neurol Neurosci Rep. 2020 Oct 30;20(12):60. doi: 10.1007/s11910-020-01079-7. Erratum in: Curr Neurol Neurosci Rep. 2020 Nov 12;20(12):66. PMID: 33128130; PMCID: PMC7599061.

Ophthalmic Complications of Covid-19

Ophthalmic Complications of Covid-19

Ocular surface disease

Orbital disease- cellulitis, opportunistic mucormycosis, dacryoadenitis, retro-orbital pain, orbital myositis

Uveitis, vitritis

Retinal disease- ischemic, hemorrhagic, acute necrosis from reactivated herpesvirus, papillophlebitis, acute macular neuroretinopathy (AMN), paracentral acute middle maculopathy (PAMM), endophthalmitis, candida retinitis, choroidal abscess, central serous chorio-retinopathy

Neuro-ophthalmic findings

Dr. Attapon Cheepsattayakorn. "**Ophthalmological Post-Acute-COVID-19-Illness Sequelae**" MAR Pulmonology 3.3 www.medicalandresearch.com (pg. 8)

Dinkin M, Segal D, Zyskind I, Oliveira C, Liu G. **Bilateral Optic Disc Edema in Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19.** Journal of Neuro-Ophthalmology: Accepted for publication. https://journals.lww.com/jneuro-ophthalmology/Documents/Covid-19%20Early%20Posting%20Collection/Bilateral%20Optic%20Disc%20Edema%20in%20Multisystem%20Inflammatory%20Syndrome%20in%20Children%20(MIS-C)%20Associated%20with%20COVID-19.pdf Accessed 11 January 2022.

Lin, Timothy P.H. MBChB∗; Ko, Chung-Nga PhD†; Zheng, Ke MD‡; Lai, Kenny H.W. FCOphthHK, FHKAM(Ophthalmology)∗,†; Wong, Raymond L.M. FCOphthHK, FHKAM(Ophthalmology)∗,†; Lee, Allie FCOphthHK, FHKAM(Ophthalmology)§; Zhang, Shaochong MD||; Huang, Suber S. MD, MBA¶,#; Wan, Kelvin H. MBChB, MRCS∗; Lam, Dennis S.C. MD, FRCOphth∗∗ **COVID-19: Update on Its Ocular Involvements, and Complications From Its Treatments and Vaccinations**, Asia-Pacific Journal of Ophthalmology: November-December 2021 - Volume 10 - Issue 6 - p 521-529 doi: 10.1097/APO.0000000000000453

Doria M. Gold, Steven L. Galetta, **Neuro-ophthalmologic complications of coronavirus disease 2019 (COVID-19)**, Neuroscience Letters, Volume 742, 2021, 135531, ISSN 0304-3940, https://doi.org/10.1016/j.neulet.2020.135531.

Nagy, Z. Z. " **Ophthalmic signs and complications of the COVID-19 infection**". Developments in Health Sciences 3.4 (2021): 79-82. < https://doi.org/10.1556/2066.2021.40001>. Web. 13 Jan. 2022.

Hu K, Patel J, Swiston C, et al. **Ophthalmic Manifestations Of Coronavirus (COVID-19)** [Updated 2022 Jan 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK556093/

Ordás, C.M., Villacieros-Álvarez, J., Pastor-Vivas, AI. et al. **Concurrent tonic pupil and trochlear nerve palsy in COVID-19.** J. Neurovirol. 26, 970–972 (2020). https://doi.org/10.1007/s13365-020-00909-1

Goyal M, Murthy SI, Annum S. **Retinal manifestations in patients following COVID-19 infection: A consecutive case series**. Indian J Ophthalmol. 2021;69(5):1275-1282. doi:10.4103/ijo.IJO_403_21

Rho J, Dryden SC, McGuffey CD, Fowler BT, Fleming J. **A Case of Non-Arteritic Anterior Ischemic Optic Neuropathy with COVID-19.** *Cureus*. 2020;12(12):e11950. Published 2020 Dec 7. doi:10.7759/cureus.11950

Neuro-Ophthalmic Complications of Covid-19

diplopia

cranial nerve palsy,

cranial nerve inflammation

myasthenia gravis

neuromyelitis optica

multiple sclerosis

ophthalmic artery occlusion

ischemic optic neuropathy

Adie's tonic pupil

ptosis

papilledema

pseudotumor cerebri

oscillopsia,

opsoclonus

myoclonus ataxia syndrome

atypical nystagmus

other eye movement disorders,

visual field defects,

visual snow,

hallucinatory palinopsia,

cortical visual impairment,

vestibular neuritis,

central vestibular nystagmus

Acute isolated near vision problems

Umapathi T, Li KZ, Chin CF, et al. **Acute Isolated Near Vision Difficulty in Patients With COVID-19 Infection**. J Neuroophthalmol. 2021;41(3):e279-e282. doi:10.1097/WNO.0000000000001120

Safarpour Lima B, Mohammadi Khorasani N, Aghamiri SH, Omidi F, Nilipour Y. **Neurological Complications of COVID-19: A Rare Case of Bilateral Blindness**. J Emerg Med. 2021 Dec;61(6):e160-e163. doi: 10.1016/j.jemermed.2021.07.035. Epub 2021 Jul 19. PMID: 34518048; PMCID: PMC8286872.

Atum M, Demiryürek BE. **Sudden bilateral vision loss in a COVID-19 patient: A case report**. Indian J Ophthalmol. 2021;69(8):2227-2228. doi:10.4103/ijo.IJO_3706_20

Selvaraj V, Sacchetti D, Finn A, Dapaah-Afriyie K. **Acute Vision Loss in a Patient with COVID-19**. R I Med J (2013). 2020 Jun 10;103(6):37-38. PMID: 32545925. https://pubmed.ncbi.nlm.nih.gov/32545925/

Amparo Ortiz-Seller, Lucía Martínez Costa, Antonio Hernández-Pons, Elia Valls Pascual, Alicia Solves Alemany & Mara Albert-Fort (2020) **Ophthalmic and Neuro-ophthalmic Manifestations of Coronavirus Disease 2019 (COVID-19)**, Ocular Immunology and Inflammation, 28:8, 1285-1289, DOI: https://10.1080/09273948.2020.1817497

Ferrucci R, Dini M, Groppo E, Rosci C, Reitano MR, Bai F, Poletti B, Brugnera A, Silani V, D'Arminio Monforte A, Priori A. **Long-Lasting Cognitive Abnormalities after COVID-19**. Brain Sciences. 2021; 11(2):235. https://doi.org/10.3390/brainsci11020235

Marsiglia, Marcela MD, PhD; Chwalisz, Bart K. MD; Maher, Mary MD. **Neuroradiologic Imaging of Neurologic and Neuro-Ophthalmic Complications of Coronavirus-19 Infection** Journal of Neuro-Ophthalmology: December 2021 - Volume 41 - Issue 4 - p 452-460 doi: 10.1097/WNO.0000000000001454

Poursadeghfard, M., Sharifian-Dorche, M., Nemati, A., & Mowla, A. (2021). **Simultaneous Encephalitis and Neuroretinitis After COVID-19 in a Young Adult: A Case Report**. Journal Of Neurology Research, 11(5), 102-107. J Neurol Res. 2021;11(5):102-107 doi: https://doi.org/10.14740/jnr698

Marsiglia M, Chwalisz BK, Maher M. **Neuroradiologic Imaging of Neurologic and Neuro-Ophthalmic Complications of Coronavirus-19 Infection**. J Neuroophthalmol. 2021;41(4):452-460. doi:10.1097/WNO.0000000000001454

Tisdale, Alanna K. MD, MPH; Dinkin, Marc MD; Chwalisz, Bart K. MD **Afferent and Efferent Neuro-Ophthalmic Complications of Coronavirus Disease 19**, Journal of Neuro-Ophthalmology: June 2021 - Volume 41 - Issue 2 - p 154-165 doi: 10.1097/WNO.0000000000001276

Suggested Mechanisms

Post-viral inflammatory syndrome

Sequelae of a pro-inflammatory state with hypercoagulability and cytokine storm

Systemic abnormalities including hypoxia and severe hypertension

Endothelial dysfunction

Direct viral neurotropism

Post-Acute Sequelae of Covid-19 (aka Long Covid)

Chen Chen, Spencer R. Haupert, Lauren Zimmermann, Xu Shi, Lars G. Fritsche, Bhramar Mukherjee, **Global Prevalence of Post-Acute Sequelae of COVID-19 (PASC) or Long COVID: A Meta-Analysis and Systematic Review**, medRxiv 2021.11.15.21266377; doi: https://doi.org/10.1101/2021.11.15.21266377

Proal AD, VanElzakker MB. **Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms**. *Front Microbiol*. 2021;12:698169. Published 2021 Jun 23. doi:10.3389/fmicb.2021.698169

Potential Mechanisms

Acute viral injury to organs

Persistent viral reservoirs in various tissues

Re-activation of neurotrophic pathogens (e.g. herpesvirus) secondary to immune dysregulation

Interactions of SARS-CoV-2 with host microbiome/virome

Clotting/coagulation issues

Dysfunctional brainstem/vagus nerve signaling

Ongoing activity of primed immune cells

Autoimmunity

Lu Y, Li X, Geng D, Mei N, Wu PY, Huang CC, Jia T, Zhao Y, Wang D, Xiao A, Yin B. **Cerebral Micro-Structural Changes in COVID-19 Patients - An MRI-based 3-month Follow-up Study**. EClinicalMedicine. 2020 Aug;25:100484. doi: 10.1016/j.eclinm.2020.100484. Epub 2020 Aug 3. PMID: 32838240; PMCID: PMC7396952.

Proal AD, VanElzakker MB. **Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms**. *Front Microbiol*. 2021;12:698169. Published 2021 Jun 23. doi:10.3389/fmicb.2021.698169

Observed Abnormalities

Gray matter changes

White matter changes

Microclot formation

Infection of cerebrovascular endothelium, brain parenchyma, neurons, and glia

Increased cytokine serum levels

Diffuse brain atrophy

Increased CSF volume

Pretorius, Resia. **Could microclots help explain the mystery of long Covid?** https://www.theguardian.com/commentisfree/2022/jan/05/long-covid-research-microclots 5 Jan 2022

Aghagoli, G., Gallo Marin, B., Katchur, N.J. et al. **Neurological Involvement in COVID-19 and Potential Mechanisms: A Review**. Neurocrit Care 34, 1062–1071 (2021). https://doi.org/10.1007/s12028-020-01049-4

Gwenaëlle Douaud, Soojin Lee, Fidel Alfaro-Almagro, Christoph Arthofer, Chaoyue Wang, Paul McCarthy, Frederik Lange, Jesper L.R. Andersson, Ludovica Griffanti, Eugene Duff, Saad Jbabdi, Bernd Taschler, Anderson M. Winkler, Thomas E. Nichols, Rory Collins, Paul M. Matthews, Naomi Allen, Karla L. Miller, Stephen M. Smith. **Brain imaging before and after COVID-19 in UK Biobank**. medRxiv 2021.06.11.21258690; doi: https://doi.org/10.1101/2021.06.11.21258690

Persistent Symptoms

Headaches

Vision changes

Hearing loss

Lost of taste or smell

Impaired mobility

Numbness in extremities

Tremors

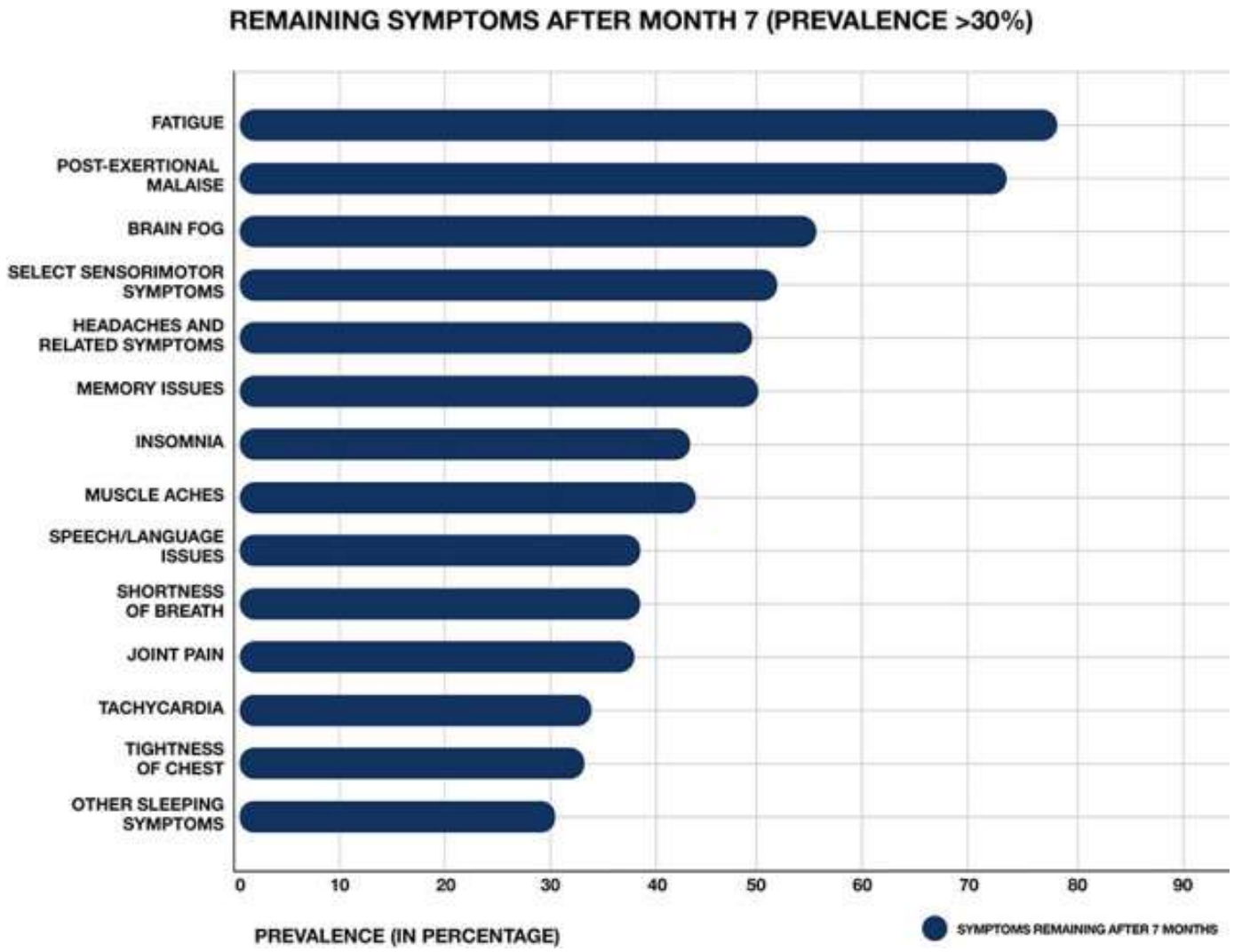
Myalgia

Memory loss

Cognitive deficits

Mood changes

Anxiety and depression


REMAINING SYMPTOMS AFTER MONTH 7 (PREVALENCE >30%)
FATIGUE
POST-EXERTIONAL MALAISE
BRAIN FOG
SELECT SENSORIMOTOR SYMPTOMS
HEADACHES AND RELATED SYMPTOMS
MEMORY ISSUES
INSOMNIA
MUSCLE ACHES
SPEECH/LANGUAGE ISSUES
SHORTNESS OF BREATH
JOINT PAIN
TACHYCARDIA
TIGHTNESS OF CHEST
OTHER SLEEPING SYMPTOMS
0
10
20
30
40
50
60
70
80
90
PREVALENCE (IN PERCENTAGE)
SYMPTOMS REMAINING AFTER 7 MONTHS

Cognitive Deficits

Global cognition

Word learning

Verbal recall

Attention

Concentration

Phonemic fluency

Category fluency

Memory (encoding and recall)

Processing speed

Visual construction

Reasoning

Problem-solving

Spatial planning

Target detection

Executive function

Adam Hampshire, William Trender, Samuel R Chamberlain, Amy Jolly, Jon E. Grant, Fiona Patrick, Ndaba Mazibuko, Steve Williams, Joseph M Barnby, Peter Hellyer, Mitul A Mehta, **Cognitive deficits in people who have recovered from COVID-19 relative to controls: An N=84,285 online study,** EClinicalMedicine doi: 10.1016/j.eclinm.2021.101044

Marcel S Woo, Jakob Malsy, Jana Pöttgen, Susan Seddiq Zai, Friederike Ufer, Alexandros Hadjilaou, Stefan Schmiedel, Marylyn M Addo, Christian Gerloff, Christoph Heesen, Julian Schulze Zur Wiesch, Manuel A Friese, **Frequent neurocognitive deficits after recovery from mild COVID-19**, *Brain Communications*, Volume 2, Issue 2, 2020, fcaa205, https://doi.org/10.1093/braincomms/fcaa205

Graham, E.L., Clark, J.R., Orban, Z.S., Lim, P.H., Szymanski, A.L., Taylor, C., DiBiase, R.M., Jia, D.T., Balabanov, R., Ho, S.U., Batra, A., Liotta, E.M. and Koralnik, I.J. (2021), **Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers".** Ann Clin Transl Neurol, 8: 1073-1085. https://doi.org/10.1002/acn3.51350

Adam Hampshire, William Trender, Samuel R Chamberlain, Amy E. Jolly, Jon E. Grant, Fiona Patrick, Ndaba Mazibuko, Steve CR Williams, Joseph M Barnby, Peter Hellyer, Mitul A Mehta, **Cognitive deficits in people who have recovered from COVID-19,** EClinicalMedicine, Volume 39, 2021, 101044, ISSN 2589-5370, https://doi.org/10.1016/j.eclinm.2021.101044.

“Clinical Spectrum of SARS-CoV-2 Infection” NIH Covid-19 Treatment Guidelines, https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/ Accessed 11 January 2022.

Gwenaëlle Douaud, Soojin Lee, Fidel Alfaro-Almagro, Christoph Arthofer, Chaoyue Wang, Paul McCarthy, Frederik Lange, Jesper L.R. Andersson, Ludovica Griffanti, Eugene Duff, Saad Jbabdi, Bernd Taschler, Anderson M. Winkler, Thomas E. Nichols, Rory Collins, Paul M. Matthews, Naomi Allen, Karla L. Miller, Stephen M. Smith. **Brain imaging before and after COVID-19 in UK Biobank**. medRxiv 2021.06.11.21258690; doi: https://doi.org/10.1101/2021.06.11.21258690

Jonas A Hosp, Andrea Dressing, Ganna Blazhenets, Tobias Bormann, Alexander Rau, Marius Schwabenland, Johannes Thurow, Dirk Wagner, Cornelius Waller, Wolf D Niesen, Lars Frings, Horst Urbach, Marco Prinz, Cornelius Weiller, Nils Schroeter, Philipp T Meyer, **Cognitive impairment and altered cerebral glucose metabolism in the subacute stage of COVID-19**, *Brain*, Volume 144, Issue 4, April 2021, Pages 1263–1276, https://doi.org/10.1093/brain/awab009

Becker JH, Lin JJ, Doernberg M, et al. **Assessment of Cognitive Function in Patients After COVID-19 Infection**. JAMA Netw Open. 2021;4(10):e2130645. https://doi.org/10.1001/jamanetworkopen.2021.30645

Jaywant, A., Vanderlind, W.M., Alexopoulos, G.S. *et al.* **Frequency and profile of objective cognitive deficits in hospitalized patients recovering from COVID-19**. *Neuropsychopharmacol.* **46,** 2235–2240 (2021). https://doi.org/10.1038/s41386-021-00978-8

Prescription

Distance:

OD -3.00 sph 0.5 Δ Base In

OS -2.75-0.25 x 090 0.5 Δ Base In 0.25 Δ Base Down

Near:

OD -2.00 sph 0.5 Δ Base In

OS -1.75-0.25 x 090 0.5 Δ Base In 0.25 Δ Base Down

Binasal Occlusion applied to both pairs at follow-up 2 weeks later.

Prescription

Syntonics:

Pi omega 5 minutes

Upsilon omega D 5 minutes

Vision Rehabilitation:

Start with 25-minute sessions once per week

Yoked prism, eye and head swings, slow tracking, peripheral hand motion, TLR, head laser, VOR cancellation

Progress Evaluation December 2021

Headaches are less intense, no longer daily (3 or 4 days/week); usually only at end of day

Able to achieve more- can tolerate grocery stores, playing Frisbee with his kids

Reduced oscillopsia- notices a greater reduction immediately after VT sessions

Still has fatigue and requires a nap most days

Reading is still problematic, but can read longer than before

Still uncomfortable as a car passenger- triggered by lights of other vehicles

Progress Evaluation December 2021

Visual Acuity with Habitual Rx: 20/20 distance and near

Convergence Near Point: 8” (but discomfort at 12”) with OD exo

Maddox rod 5 Δ BI, no vertical

Stereo 50 sec with distance Rx; 40 sec with near Rx

OKN drum sensitivity: 1/5 in left and right quadrants; 0/5 in upper and lower quadrants

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