Brain Fog and Cognitive disorders in The Vaccine Injured

The Tsunami is Here



There is Tremendous Fall Out to the Brain Post COVID and Post Vaccine

- Spike protein is a dangerous neurotoxin with the brain as possibly its primary target to take down
- The CDC says 1 in 5 has Long COVID
- 72.4% percent of the world's population received at least one dose of the COVID vaccine or 5.55 billion people as of March 2023 (NYT)

A Tsunami of Disability Is Coming as a Result of 'Long COVID' Scientific American 2021 Massive health-record review links viral illnesses to brain disease Nature 2023



A Very Scary Mass Disabling Event

- Research has shown that even mild SARS COV 2 can have lasting effects on the brain and body
- 762,201,169 confirmed cases of COVID-19 have been reported (April 5,2023 WHO), including 6,893,190 deaths
- 65 million are suffering with "Long COVID" world-wide (Davis 2023)
- Most are between the ages of 36 and 50 years that had mild COVID
- Millions more Americans are disabled

Long COVID: Major findings, Mechanisms and Recommendations Davis H et al Nature Reviews Jan 2023



A Very Scary Mass Disabling Event

- In this recent study from Brazil, they found marked difficulty with constructional skills with visuospatial impairment (average age was 38)
- 1 in 4 have Cognitive Deficits
- On MRI they had large volumes c/w neuroinflammation and in high inflammatory cytokines in blood
- Constructional apraxia can be an early sign of neurodegenerative disease

Selective visuoconstructional impairment following mild COVID-19 with inflammatory and neuroimaging correlation findings Jardim de Paula J et al Molecular Psychiatry 2023

Constructional Apraxia as a Distinctive Cognitive and Structural Brain Feature of Pre-Senile Alzheimer's Disease Serra L J of Alzheimer's Disease 2014



Meaning: impaired visuospatial ability = cognitive deficit

#58N22

Marco Romano-Silva and colleagues found 1 in 4 people with mild COVID-19 struggled to draw the ROCF, indicating significant cognitive impairment in visuoconstruction skills.

Marco Romano-Silva

How many are Vaccine Injured?

- The Rassmusen report (March 2023) 10% said someone in their household died from the vaccine and 11% said someone died from COVID-19 (VAX=Virus?) A prior survey showed 7% have major side effects after vaccine
- V-Safe Data : 7.7% seek medical care after vaccination and 33% have serious side effects
- A study by Doshi et al, found the risk of a serious adverse event in 1 in 800
- A study by Fraiman J et al, Vaccine. 2022, serious risk was 1 in 550 individuals



How Many are Vaccine Injured?

- 13 million killed world-wide (Rancourt D et al 2023)
- 278000 killed or 1 out of 874 persons killed by Covid vaccines (Skidmore 2023 survey from Dec 2021-Dec 2022
- Vaccinated had a 14% higher mortality (Šorli A March 2023)
- A recent report from the research firm Phinance Technologies, found the total "economic cost" of \$147.8 billion in 2022 due to the Covid-19 vaccines with 300k excess deaths and 26.6 million injured (March 2023)

Age-stratified COVID-19 vaccine-dose fatality rate for Israel and Australia Rancourt D et al Research gate Feb 2023

Forgotten "Primum Non Nocere" and Increased Mortality after COVID-19 Vaccination (Šorli A et al Quality in Primary Care March 2023



http://www.phinancetechnologies.com

The Canary in the Coal Mine

 The cumulative toxic effect on neurological tissue from chronic exposure to lingering spike protein and repeated periodic injections is not known. The canary in the coal mine will be paying close attention to any rise in neurodegenerative disorders.



NEUROSCIENCE

Long COVID Now Looks like a Neurological Disease, Helping Doctors to Focus Treatments

The causes of long COVID, which disables millions, may come together in the brain and nervous system



Credit: Stephanie Shafer

Trust the Science

 In 1949, the Portuguese neurologist António Egas Moniz received the Nobel Prize in medicine for his development of the prefrontal lobotomy



Report 57: 542 Neurological Adverse Events, 95% Serious, in First 90 Days of Pfizer mRNA Vaccine Rollout. 16 Deaths

- 376 seizures were reported, twelve of which were "status epilepticus," a rare condition of prolonged seizure or series of seizures that is life-threatening
- 38 cases of multiple sclerosis and 10 cases of optic neuritis
- 11 cases of transverse myelitis
- 24 cases of Guillain-Barré syndrome
- 3 cases of meningitis
- 7 cases of encephalopathy
- Never Safe and Never Effective with clinical trial data to be hidden X 75 years
- No preclinical safety studies for genotoxicity, oncogenicity, or teratogenicity





Lipid Nanoparticles: Are They Safe?

- LNPs in which the mRNA is encapsulated should have very restricted distribution targeting the draining axillary lymph nodes, but studies have shown high IgG antibodies to S1 in CSF post vaccination (Malin M 2022) (Coley M 2023)
- The Pfizer biodistribution study showed high levels of LNP's in the liver, spleen, adrenal glands, bone marrow and ovaries
- LNPs easily cross the BBB and are highly inflammatory (Cena V 2018) (Moghimi S 2022)
- PEG caused enhancement of amyloid in mice (Mambule C 2000) and suggest LNP's may increase risk of NDG disease



A Lasting Legacy

 The mRNA-LNP vaccine platform induces longterm unexpected immunological changes affecting both adaptive immune responses and heterologous protection against infections that can be passed down to future generations (Quin Z)

Pre-exposure to mRNA-LNP inhibits adaptive immune responses and alters innate immune fitness in an inheritable fashion Qin Z POLS Pathogens 2022

Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line Alden M et al Curr. Issues Mol. Biol. 2022



Children of Stephen and Annie Dunn Front: Lora Annie, John Anthony, Katherine Elizabeth, James Steven, Gussie Agnes Back: Mary Louise, Clarence Timothy, Cecilia Eva and Patrick

A Lasting Legacy

- SARS-CoV-2 RNA, can be reverse transcribed by LINE-1and then synthesized DNA can become integrated at unknown frequencies and locations into the vaccinees' genomes. (Alden M et al 2022)
- What is the lasting legacy we are leaving if ultimately mRNA is incorporated into germ cell DNA for transgenerational transmission??

Pre-exposure to mRNA-LNP inhibits adaptive immune responses and alters innate immune fitness in an inheritable fashion Qin Z POLS Pathogens 2022

Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line Alden M et al Curr. Issues Mol. Biol. 2022



Trojan Horses with toxic cargo of S1: How Long Does it Linger and Why ?

- Spike protein found in nonclassical monocytes up to 15 months (Patterson et al)
- Spike protein is found in exosomes up to four months (Bansal S et al)
- Spike protein also has been found in plasma a year post infection (Swank Z), on thrombi (DeMichelle M), heart muscle (Yonker L), skin cells (Yamanoto M) brain (Mörz M) liver (Schroff H) bone marrow (Rong Z 2023)
- 30% of PASC patients were positive for both mRNA and S1 but 100% were positive for S1 (Craddock V 2023)
- mRNA lingers too in CSF, lymph nodes, breast milk and in muscle tissue (Cradock V) (Reinhold D) (Alden M) (Viszlayova D) (Röltgen, K.)



The Haunting of Spike Protein Induced Disease

- Endothelial dysfunction/vascular inflammation and clotting (Trougakos I et al)
- Can cross and damage the blood-brain barrier (Rhea et al)/ activates microglia, causes neuroinflammation & death of the brain
- Binds to the ACE 2 receptor can induce renin-angiotensinsystem (RAS) imbalance and inflammation
- Damages mitochondria (Clough E et al)
- May change genetic expression (Alden M 2022)
- Molecular mimicry to many human tissues and cells (Vojdani 2021)



The Haunting of Spike Protein Induced Disease

- Alteration of immune health and generates high levels of inflammatory cytokines (Seneff 2022)
- Fuels protein misfolding/prion formation (Nystrom et al 2022)
- S1 contains neurotoxins (Rivas M 2022)
- S1 can suppress the nicotinic Ach system (Zafa L et al 2022)
- Advances senescence and shuts down autophagy
- Viral reactivation (Vojdani A 2023)
- Gut destruction (Hazan S 2022, 2023)
- Mast Cell Activation (Arun S 2022)



The brain under attack in Long COVID and Vaccine Injuries

A Neurological Crisis



Most Common Neurological Diagnosis after the Vaccine



- Undefined/ Novel Neurological Syndromes
- Cognitive impairment
- Cortical Vein Thrombosis
- CNS demyelinating disorders (TM, ADEM, MS, NMOSD)
- Encephalitis
- Seizures
- CVA
- GBS / CIDP/ Small Fiber Neuropathy
- Bells Palsy
- Movement Disorders
- Neuromuscular Syndromes
- Headache, fatigue, malaise
- Intracranial Aneurysm rupture
- Tinnitus

COVID-19 Vaccination and Neurological Manifestations: A Review of Case Reports and Case Series Wen S et al Brain Sci. 2022 Mar

Spike Protein Damages the BBB The Gatekeeper to the Brain

- Spike protein promotes loss of BBB integrity and triggers an inflammatory response in brain endothelial cells by binding to the ACE 2 receptors and through adsorptive mediated transcytosis and then is taken up into the brain tissue (Rhea E 2020)
- A study, performed at the NIH (July 2022) showed antibodies induced by spike protein attacking the endothelial cells of the BBB (Nath A 2022)
- The BBB is disrupted in Long COVID (Green C 2023)

The SARS-CoV-2 spike protein alters barrier function in 2D static and 3D microfluidic in-vitro models of the human bloodbrain barrier Buzhdygan T et al Neurobiol of Disease October 2020

Rhea E et al S1 protein of SARS-CoV-2 crosses the blood-brain barrier in mice. Nature Neuroscience, 2020 Blood-brain barrier disruption in Long COVID-associated cognitive impairment Green C Research Square 2023



n of a microvessel in the brain lined by the blood-brain barrier. The arrier is a multicellular, compound structure composed of endotheli es and astrocytes in direct contact with brain tissue.

https://commons.wikimedia.org/wiki/File:Blood_vessels_brain_eng

Protective Barriers?

- Meninges are three layers of membranes that cover and protect your brain and spinal cord and they carry a rich vascular network
- Meninges host a rich repertoire of immune cells mediating CNS immune surveillance and are part of the BBB
- Spike protein has been found in skull marrow, meninges and brain (Rong Z 2023)

Skull and vertebral bone marrow are myeloid cell reservoirs for the meninges and CNS parenchyma Cugurra A et al Science 2021

SARS-CoV-2 Spike Protein Accumulation in the Skull-Meninges- Brain Axis: Potential Implications for Long-Term Neurological Complications in post-COVID-19 Rong Z bioRxIV March 2023



Bone Marrow and Spike Protein

- Post COVID or Post vaccine we see alteration of changes in blood counts
- S1 has been found to interact with ACE 2 receptors in the bone marrow (Zheng B 2021)
- Severe aplastic anemia (Tabata 2022), autoimmune hemolytic anemia (Fatima 2022) bone marrow suppression (Shastri 2022), and damage to the hematopoietic stem/progenitor cells (Kucia 2021)
- The Pfizer biodistribution study, showed high levels of LNP's were found in the liver, bone marrow, spleen and ovaries

COVID-19 vaccines and risks of hematological abnormalities: Nested case–control and self-controlled case series study Sing C et al J of Hematology 2022

An evidence that SARS-Cov-2/COVID-19 spike protein (SP) damages hematopoietic stem/progenitor cells in the mechanism of pyroptosis in NIrp3 inflammasome-dependent manner Kucia M et al Leukemia June 2021

https://www.naturalnews.com/files/Pfizer-bio-distribution-confidential-document-translated-to-english.pdf

Bone Marrow Basics



Spike Protein Lingering in the Body, Skull and Brain

- In the rats injected with spike protein, most organs, including the heart, lung, liver, kidney, intestine, thymus, spleen, pancreas, testis and ovaries, brain frontal cortex, skull marrow, & meninges all showed spike protein
- In the brains, only spike, no nucleocapsid and all were PCR negative
- Spike protein may linger for a long time and was even found in the skull marrow a subset of individuals who recovered from COVID-19 and did not die from COVID
- Spike protein persistence may contribute to long-term neurological symptoms and may have a long lifetime in the body and brain

SARS-CoV-2 Spike Protein Accumulation in the Skull-Meninges- Brain Axis: Potential Implications for Long-Term Neurological Complications in post-COVID-19 Rong Z bioRxIV March 2023





We Have Only Begun To See What Spike Protein Will Do to the Brain

- Spike protein causes death of brain cells, activates complement & coagulation pathways, brain inflammation and risk of stroke/ bleeding
- Spike protein was associated with a broad spectrum of proteome changes like neutrophil-related pathways ,dysregulation of the PI3K-AKT pathway (tumor growth) & complement and coagulation pathways
- Proteome changes which are associated with neurodegeneration

SARS-CoV-2 Spike Protein Accumulation in the Skull-Meninges- Brain Axis: Potential Implications for Long-Term Neurological Complications in post-COVID-19 Rong Z bioRxIV March 2023



Microglia

 The Brain Has about 100-200 billion microglia that work to protect the brain and create a symphony of neuronal circuits



Damage to the BBB Leads to Chronic Neuroinflammation : The Downfall of the Brain

- Activation of the microglia
- Increasing Oxidative Stress
- High levels of Glutamate
- Reduction of astrocytic glutathione
- Further damage to the BBB
- Mitochondria, micro-vessels, proteosomes, cell membranes, nuclear and mitochondrial DNA are all caught in the crossfire
- Prion formation





Rainbow bright: The brain of an individual with autism (bottom) shows more activated microglia than a control brain does (top).

Spike protein activates TLR4 and then microglia and drives neuroinflammation

- SARS-CoV-2 Spike protein stimulates release of pro-inflammatory cytokines from cultured microglia through TLR4 receptor activation (Zhao Y 2021) (Fontes-Dantas 2022 & 2023)
- TLR4 has been implicated in microglial activation and cognitive dysfunction in neurodegenerative chronic disease

Recombinant SARS-CoV-2 Spike Protein and its Receptor Binding Domain stimulate release of different pro-inflammatory cytokines of distinct receptors on microglial cells T Theoharides et al Research Square Jan 2023

SARS-CoV-2 spike protein induces TLR-4-mediated long-term cognitive dysfunction recapitulating post-COVID syndrome Fontes-Dantas F et al Cell Rep 2023

Y. Zhao et al SARS-CoV-2 spike protein interacts with and activates TLR41.Cell Res. (2021)

Microglia can assume various states of activation.



Spike protein stimulates pro-inflammatory mediators via activation of microglial cells and drives neuroinflammation

- A Recent paper demonstrates that exposure to Spike protein causes the destruction of synapses in the brain, neuroinflammation, memory loss, and cognitive dysfunction 30-45 days after exposure
- This neurotoxicity of the Spike protein appears to be mediated by TLR4, and is therefore a byproduct of the immune response to Spike
- It is neuroinflammation and hippocampal microgliosis that mediate Spike-induced memory dysfunction
- Spike protein alone is provoking neuroinflammation and no ACE 2 receptor or virus is required
- Sulforaphane, Curcumin, Resveratrol can downregulate TLR 4

SARS-CoV-2 spike protein induces TLR-4-mediated long-term cognitive dysfunction recapitulating post-COVID syndrome Fontes-Dantas F et al Cell Rep 2023



The NLRP3 inflammasome: The Danger Signal to the Microglia being Sparked by Spike Protein

- NLRP3 can be activated by multiple infectious triggers, prions, environmental toxins and spike protein (Frank M)
- NLRP3 is involved in neurodegenerative disease (Cui Y 2022) (Holbrook J 2021)
- Berberine , omega 3, Resveratrol, Curcumin , EGCG, Sulforaphane, Quercetin downregulate the NLRP3 inflammasome (Tőzsér 2016)

SARS-CoV-2 drives NLRP3 inflammasome activation in human microglia through spike protein Alborno E et al Nov 2022

SARS-CoV-2 spike glycoprotein S1 induces neuroinflammation in BV-2 microglia. Olajide OA. 2022



Glutamate and the NMDA receptors are Necessary for Proper Brain Function: If Impaired this Will Lead to Neurodegeneration

- Glutamate released by activated microglia induces excitoneurotoxicity and may contribute to neuronal damage in neurodegenerative disease
- S1 shares molecular mimicry with the NMDA receptor which will fuel glutamate
- N-methyl-D-aspartate (NMDA) receptor imbalance is associated with memory ,learning impairments and neuropsychiatric symptoms

Molecular mimicry of NMDA receptors may contribute to neuropsychiatric symptoms in severe COVID-19 cases Geis C et al J of Neuroinflammation 2021

Glutamate Excitotoxicity Is Involved in the Induction of Paralysis in Mice after Infection by a Human Coronavirus with a Single Point Mutation in Its Spike Protein Brison E et al J Virol. 2011



Mental Fallout after the COVID vaccine

- As of Jan 2023, there are ~10 papers describing headache, fever, and a range of acute neuropsychiatric symptoms including suicide after both mRNA and adenoviral COVID-19 vaccination
- We are experiencing a mental health epidemic
- Suicides and homicides spiked in 2021 and are rising

First Episode of Psychosis Following the COVID 19 vaccination- A Case Series Borovina T et al Psychiatria Danubina, 2022; Vol. 34, No. 2, pp 377-380

First Episode Psychosis Following COVID-19 Vaccination: a Case Report Renemane L et al Psychiatr Danub 2022 Sep;34(Suppl 8):56-59.

SARS-CoV-2 spike protein induces cognitive deficit and anxiety-like behavior in mouse via hippocampal neuronal death Oh J 2022



Sobering Evidence of Harm

- 76-year-old male patient with a history of Parkinson's disease, post-COVID vaccination X 3; who clinically deteriorated and died
- After his first vaccination in May 2021, he develop severe cardiovascular symptoms and after # 2 he had profound advancement of his neurodegenerative disease (over 3 months)
- He died 9 months after his first COVID vaccine
- Dr. Mörz's article provides compelling and sobering evidence of potential serious side effects of the mRNA vaccines

A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against COVID-19" showing chronic neuroinflammation, microglial cell activation and cell death Michael Mörz Vaccines 2022



Acute Lymphocytic Vasculitis

- Vasculitis is autoimmune induced with immune complexes deposited in vessels walls causing inflammation of the blood vessels
- CNS vasculitis can present with a variety of neurological symptoms from brain fog, confusion, seizures, neuropathy, vision changes paralysis, headache and more
- Vasculitis is associated with the SARS COV 2 vaccine (Metlar C 2022)

Mörz, M. (2022) A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against Covid-19. Vaccines 10:2022060308

Fillon, A. et al. (2022) De novo and relapsing necrotizing vasculitis after COVID-19 vaccination. Clin. Kidney J. 15:560-563



Il brain. Positive reaction for SARS-CoV-2 spike protein. Cross se (same vessel as shown in Figure 11, serial sections of 5 to 20 μ m) in for SARS-CoV-2 spike subunit 1 detectable as brown granules ed arrow) and individual glial cells (blue arrow). Magnification: 200

This Raging Indolent Immune Response is Continuing to Cause Neuronal Injury

 The slide on the Right is from a NIH study showing damage to the blood vessels in the brain due to S1 induced mediated cytotoxicity directed against the endothelial cells along the BBB. Notice the same on the left from the Mörz case



Figure 4. Brain, periventricular vasculitis. Cross section through a capillary vessel showing prominent signs of vasculitis. The endothelial cells (5) show swelling and vacoulation and are increased in number with enlargement of nuclei, indicative for activation. Furthermore, presence of mixed inflammatory cell infiltrates within the endothelial layer, consisting of lymphocytes (1), granulocytes (2), and histiccytes (4). The adjacent brain tissue also shows signs of inflammation (encephalitis) with presence of lymphocytes as well and activated microglia (3). H&E. Magnification: 200× (a) and 400× (b).



What Mörz Saw

- Chronic neuroinflammation with activation of microglia and the invasion of inflammatory cells (mainly lymphocytes). After brain injury, lymphocytes become activated, infiltrate the brain, and release cytokines and reactive oxygen species to contribute to inflammation and brain injury
- Dying neurons (Multifocal necrotizing encephalitis)
- Spike protein will bind to neurons and glial cells which express ACE2 receptors in the CNS

Mörz, M. (2022) A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against Covid-19. Vaccines 2022



Figure 2. Frontal brain. Already in the overview image (a), prominent vacuolations with increased parenchymal cellularity are evident, indicative of degenerative and inflammatory processes. At higher magnification (b), acute brain damage is visible with diffuse and zonal neuronal and glial cell death, activation of microglia, and inflammatory infiltration by granulocytes and lymphocytes. I: neuronal deaths (cells with red cytoplasm); 2: microglial proliferation; 3: lymphocytes. H&E stain. Magnification 40× (a) and 200× (b).

Alzheimer's & Spike-opathy

A rising tide of all neurodegenerative disease for years to come We will see Novel Presentations Neurodegenerative Disease Presentations may Change

- We were taught that Alzheimer's Disease begins decades before clinical presentation
- Things are changing

What are the 7 Stages of Alzheimer's Disease?



Source: Dr. Barry Reisberg of New York University

Shifting Tides Has a New Form of Alzheimer's Disease Arrived?

- People 65 and older who contracted COVID-19 were more prone to developing Alzheimer's disease in the year following their COVID diagnosis. The highest risk was observed in women at least 85 years old. (Wang 2022)
- Risk of dementia was significantly higher in the post COVID patients then controls (mean age 42.5) Taquet 2022
- People who got COVID-19 were twice as likely to receive a diagnosis of Alzheimer's disease in the 12 months after infection (Nature Medicine 2022)



Shifting Tides: Has a New Form of Alzheimer's Disease Arrived?

- The UK Biobank neuroimaging study showed that even mild covid can lead to an overall reduction in the size of the brain equivalent to 10 years of aging
- 22% of patients had cognitive issues 12 weeks after infection (Davis 2023)

Association of COVID-19 with New-Onset Alzheimer's Disease Wang L et al J of Alzheimer's July 2022

Long-term neurologic outcomes of COVID-19 Xu Evan Nature Medicine Sept 2022

Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients Tauget M et al The Lancet psychiatry August 17, 2022

Long COVID: major findings, mechanisms and recommendations Davis H Nat Rev Microbiol. 2023



jerusalem Post > Health & Wellness

Could an Alzheimer's drug help children with autism?

What to know about 'childhood Alzheimer's'

Causes | Symptoms | Treatment | Risk factors | Outlook | Summary

Hundreds of Children Diagnosed With 'Childhood Dementia' - Doctors Baffled

C August 17, 2022 & Servi Dirity & Novi, US C 20 Comments



19-year-old becomes youngest ever diagnosed with Alzheimer's disease

Research challenges the established view of the disease and its association with aging

Swikar Oli

Published Feb 16, 2023 • Last updated 18 hours ago • 2 minute read

Childhood dementia: It's time to face it

Join the FACE it awareness campaign.

Bruce Willis Recently Diagnosed with FTD a Rare Prion Disease

- FTD is the most common dementia in those under age 65
- Unusual or antisocial behavior & loss of speech or language are usually the first symptoms.
- He began with language problems in 2021 while filming Wrong Place released July 2022
- A paper by Zhao et al lists 25 cases of Alzheimer's disease, epilepsy, multiple sclerosis, prion disease, and visual disturbances associated with long COVID.

Zhao Y, SARS-CoV-2, long COVID, prion disease and neurodegeneration. Front Neurosci. 2022

Bruce Willis has frontotemporal dementia: What are the symptoms of FTD?

FTD is a category of dementia that specifically affects the brain's frontal and temporal lobes and most commonly strikes those younger than 60

By Richard Sima, Kelyn Soong, Caitlin Gilbort and Marlone Cimons February 16, 2023 at 9:07 p.m. EST



Prions: The Spark that Fuels Neurodegeneration

- Many neurodegenerative diseases such as Alzheimer's, Parkinson's, Huntington's and ALS and even MS are now thought to be a result of prion-like activity
- Prions travel from cell to cell and self propagate causing more proteins to misfold & promote neuroinflammation and death of neurons
- SARS-CoV-2 is the only coronavirus with a prion-like domain found in the receptor-binding domain of the S1 region of the spike protein (Tetz G 2020)

Misfolding of Brain Proteins Triggering Neurodegenerative Diseases Westaway D : Biology, Health and Medicine Dec 2021

Is MS a Transmissible Protein Misfolding Disorder? ACTRIMS 2018 Tsutsui S University of Calgary



Spike Protein: A Recipe for Prions

- S1 causes amyloid to form (Nystrom S et al 2022)
- S1 protein binds to heparin and the heparin binding domain which accelerates amyloid in the brain. This may advance neurodegeneration (Idrees D 2021)
- S1 and other viral fragments drive senescence and block autophagy (Meyer K et al 2021)



Spike Protein: A Recipe for Prions

- Micro-clots contain amyloid and are very resistant to breakdown and these clots can propagate which suggests S1 amyloidogenic properties (Kreuger A 2022)
- Codon optimization and mistranslation w mRNA can result in protein misfolding (Seneff S 2022 & Smith K et al 2022)
- When amyloid fibrils aggregate, they nucleate and once nucleated AMYLOID AGGREGATES SELF-PROPOGATE

Self-propagation of pathogenic protein aggregates in neurodegenerative diseases Jucker M et al Nature 2013



Invading Cognitive Centers of the Brain

- In a study they by Shen et al, they looked at 17 COVID-19 vs 17 non-COVID-19 human brains (most with no h/o NDG disease)
- SARS-CoV-2 RNA, nucleocapsid, and spike proteins are present in neurons of the cognitive centers of all COVID-19 patients (no whole virus)
- These viral fragments activate microglia, causes neuroinflammation and induces A β and p-tau deposits in **non-Alzheimer's patients too**
- SARS-CoV-2 triggers AD-like gene programs in **healthy** neurons and exacerbates AD neuropathology
- The 2002 and 2012 SARS and MERS epidemics caused memory impairment in many recovered patients but not like we are seeing now

SARS-CoV-2 invades cognitive centers of the brain and induces Alzheimer's-like neuropathology Shen W et al bioRxIV Sept 2022



MRI Reveals Significant Brain Abnormalities in Cognitive Centers Post-COVID

- Researchers identified changes to the ventral diencephalon, white matter and frontal lobe 6 months after COVID-19 in 46 Long COVID patients and 30 healthy controls
- The affected brain regions are linked with fatigue, insomnia, anxiety, depression, headaches and cognitive problems.

Susceptibility-Weighted Magnetic Resonance Imaging Highlights Brain Alterations in COVID Recovered Patients Mishra S et al medRxiv preprint Nov 2022



Figure 1: Group analysis on susceptibility weighted imaging exhibiting higher SWI values (lower susceptibilities) in the COVID group when compared to healthy controls. Three significant clusters were found primarily in the white matter regions of pre-frontal cortex and in the brainstem. The clusters (a) and (b) are observed bilaterally in the cerebral white matter near the orbito-frontal gyrus whereas (c) lies in the midbrain region.

Fading Memories: Accelerating Dementia in the Most Vulnerable

- In this study from the J of Alzheimer's Disease March 2023, they found rapid progression of dementia post COVID in all subtypes and both degenerative and vascular dementias started behaving like mixed dementia both clinically and radiologically
- A rapidly and aggressively deteriorating course was observed in patients who were previously cognitively stable
- Cortical atrophy, vasculopathy in white matter were seen on MRI

The Effects of SARS-CoV-2 Infection on the Cognitive Functioning of Patients with Pre-Existing Dementia Souvik D et al J of Alzheimers 2022



This Photo by Unknown Author is licensed under CC BY-NC-ND

'FADE-IN-MEMORY'

 Based on the progression of cognitive deficits and the association with white matter intensity changes, the authors propose a new term: "FADE-IN MEMORY."

The Effects of SARS-CoV-2 Infection on the Cognitive Functioning of Patients with Pre-Existing Dementia Souvik D et al J of Alzheimers 2022



Spike Protein Modulates the Expression of Proteins That May Amplify Alzheimer's disease

- Molecular changes in brain autopsies done on patients with pre-existing dementia who died of COVID-19 compared to those who died of COVID-19 with no history of dementia
- S1 binding to vessel walls induces a proinflammatory microenvironment, damages the BBB, activates microglia and creates a hypercoagulable state stressing the dysfunctional neurons (this was 5-10X worse in those with dementia) targeting vulnerable areas
- Molecular changes in protein expression fuel neurodegeneration
- No virus or mRNA was found

The amplification of CNS damage in Alzheimer's disease due to SARS-CoV2 infection Nuovo G et al Ann Diagn Pathol Dec 2022



Spike Protein fuels Cognitive Impairment and May Worsen or Unmask Dementia

- S1 crosses the BBB & can act as an independent brain pathogen that can worsen or unmask Alzheimer's Disease
- The SARS-CoV-2 pseudovirus is taken up by microglia and it and S1 induce neuroinflammation in brain.
- Neuroinflammation induced by icv injection of S1 protein was greatly enhanced in the SAMP8 AD mouse model
- The delta and omicron variants showed the most robust uptake of spike protein by brain

Blood-brain barrier penetration of non-replicating SARS-CoV-2 and S1 Variants of Concern induce neuroinflammation which is accentuated in a mouse model of Alzheimer's disease Erickson M Brain Behavior and Immunity March 2023





A case of cerebral amyloid angiopathy related inflammation after vaccination against SARS-CoV-2 Yamakawa M et al Neuroimmunology reports 2022

- A 57y/o F presented with unilateral migraine headaches, dizziness, unsteadiness, and fogginess 36 hours after administration of mRNA vaccine
- MRI head with and without contrast showed leptomeningeal enhancement and sulcal edema more prominent on the right with a cortical microhemorrhage in the right hemisphere
- CSF negative but biopsy showed amyloid deposits in vessels
- CAA is a rare cause of subacute inflammatory cognitive decline, headaches, and seizures

Alpha7 nicotinic acetylcholine receptor expression by vascular smooth muscle cells facilitates the deposition of Abeta peptides and promotes cerebrovascular amyloid angiopathy Clifford P Brain Research 2008



aph of a blood vessel from the surface of the frontal lobe of a human brain shows how amylc a) have replaced vascular smooth muscle (red). Researchers say vessel membranes (green) (weakened—and subject to bleeding—after treatment with anti-amyloid antibodies. WILBER RO

Brain Fog and Cognitive Impairment

- Multiple studies have shown a high incidence of cognitive impairment in post-COVID-19 patients exceeding 50% in all studies
- You might as well be drinking, for, brain fog is on the same magnitude as intoxication (the UK drink driving limit) or 10 years of cognitive aging
- CSF studies have shown evidence of immune activation (antineuronal antibodies, oligoclonal bands) Frank C 2023, Apple A 2022
- We did not see this with SARS 1 or MERS (Green C , Research Square 2023)

"Brain Fog" by COVID-19 or Alzheimer's Disease? A Case Report Front Psychology Matias-Gulu J Nov 2021

Covid-19: one in three has neurological or psychiatric condition diagnosed after Covid infection, study finds. Mahase E et al BMJ. 2021

"Brain Fog" by COVID-19 or Alzheimer's Disease? A Case Report Front Psychology Matias-Gulu J Nov 2021

- Her cognitive symptoms started immediately after COVID-19 & CSF biomarkers and PET scan were highly suggestive of Alzheimer's disease
- Spike protein drives amyloid-β, tau, and TDP-43 pathology
- This case illustrates the need for a thorough assessment of patients reporting cognitive complaints after COVID-19 or after the vaccine
- SARS-CoV-2 activates ER stress and Unfolded protein response Fernandes L et al Preprint 2021
- Prion-Associated Neurodegeneration Causes Both Endoplasmic Reticulum Stress and Proteasome Impairment in a Murine Model of Spontaneous Disease 2020 International Journal of Molecular Sciences

Biomarkers for Alzheimer's

- PrecivityAD™
- Quest AD Detect : Ratio of AB 40 to 42 Higher risk of AD: < 0.160
- APO E genotype 4 indicates the highest risk
- plasma P-tau217 (coming soon)
- The exact role that APOE plays in the development and progression of Alzheimer's is not clear, but it is associated with the production and elimination of amyloid beta in the brain.

- Bollinger, J, et al. Validation of plasma amyloid- β 42/40 for detecting alzheimer disease amyloid plaques. Neurology Dec 2021

Prediction of Longitudinal Cognitive Decline in Preclinical Alzheimer Disease
Using Plasma Biomarkers Mattson-Calgren N JAMA Neurology 2023

What if You Knew Alzheimer's Was Coming for You?

Simple blood tests may soon be able to deliver alarming news about your cognitive health.

The Brain Under Assault and Brain Fog

- Multiple factors appear to contribute to the SARS-CoV-19 spike protein induced pathophysiology known as "brain fog". These can include microthrombi, stroke, vasculitis, high levels of inflammatory cytokines, misfolded proteins, miRNA charged exosomes inducing microglial inflammation, activation of the kynurenine pathway, compromised mitochondrial function, apoptosis, anti-neuronal antibodies, elevated glutamate, break down of the BBB and high levels of neuroinflammation
- Spike protein influences cell signaling including MAPK signaling which are involved in all major neurodegenerative diseases

SARS-CoV-2 Spike Protein Elicits Cell Signaling in Human Host Cells: Implications for Possible Consequences of COVID-19 Vaccines Suzuki Y et al Vaccines 2021

Blood-brain barrier disruption in Long COVID-associated cognitive impairment Green C Research Square 2023

Risk factors and abnormal cerebrospinal fluid associate with cognitive symptoms after mild COVID-19 Jan 2022 Annals of Clinical and Translational Neurology

More Spike Protein Uncanny Surprises

- There is uncanny similarity of 4 unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 (Pradhan P 2020) These are not found in other coronaviruses
- S1 and Gp120 function similarly , they are both peptides that can cross the BBB
- Gp120 is toxic to the hippocampal neurons and is involved in the pathogenesis of HIV-1-associated neurocognitive disorders (HAND)

Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag $\,$ Pradham P bioRX 2020 $\,$

Target of HIV-1 Envelope Glycoprotein gp120–Induced Hippocampal Neuron Damage: Role of Voltage-Gated K+ Channel Kv2.1 (2015) Zhu Q Viral Immunol. 2015

Figure 3. Modelled homo-trimer spike glycoprotein of 2019-nCoV virus. The inserts from HIV envelop protein are shown with colored beads, present at the binding site of the protein.

Damage to the Brain's Super-Highway

- 100% of people developed CNS demyelination of the optic nerve, brain, and/or spinal cord within 1-21 days post vaccine (Khayat-Khoei 2022)
- Chemo-Brain and Post COVID Brain Fog are similar with damage to the white matter and hippocampus (Monje 2022)
- Myelin shares molecular mimicry with S1 (Vojdani 2021)

Is Long COVID and Spike-opathy a New Form of Jutoimmune Disease

More research suggests spike protein looks eerily like the body and brain

Mallory Stanislawczyk sits with her daughter Olivia, 3, while receiving a saline infusion at her Walkersville,

The Brain is Being Injured by Not So Friendly Fire

- S1 reacts with 25 proteins linked with Alzheimer's disease & 43 proteins linked to Parkinson's disease (Yapic-Eser H 2021)
- In the Vojdani study 2021, spike protein shared molecular mimicry with amyloid, tau, synuclein, myelin and axons
- Alzheimer's Disease is now being looked at as an autoimmune disease

Alzheimer's disease as an innate autoimmune disease (AD2): A new molecular paradigm Weaver D Alzheimer's Dementia Sept 2020

Functional autoantibodies in patients with different forms of dementia Plus One 2018

Neuropsychiatric Symptoms of COVID-19 Explained by SARS-CoV-2 Proteins' Mimicry of Human Protein Interactions Yapic-Eser H et al Front. Hum. Neurosci., March 2021

Functional autoantibodies against G-protein coupled receptors in patients with persistent Long-COVID-19 symptoms. Wallukat G et al Journal of Translational Autoimmunity 2021

Snake Venom Neurotoxins Found in Spike Protein

- Neurotoxins in S1 block nicotinic ach receptors and impair this critical cholinergic pathway needed for neuromodulation and critical network interactions (Rivas M 2022, Ruzafa LR 2023)
- The cholinergic system receptors are neuroprotective and anti-inflammatory & if impaired many symptoms can occur (muscle weakness or fatigue, cramps fasiculations, tremor, movement disorders, memory issues)

Nicotinic Acetylcholine Receptor Involvement in Inflammatory Bowel Disease and Interactions with Gut Microbiota Ruzafa LR et al Int J Environ Res Public Health. 2021

Multisystem Inflammatory Syndrome in Children and Long COVID: The SARS-CoV-2 Viral Superantigen Hypothesis Rivas M Frontiers of Immunology July 2022

A cartoon from a December 1894 antivaccination publication (Courtesty of The Historical Medical Library of The College of Physicians of Philadelphia)

The Evolving ? Brain

- Our human brain evolved in a linear fashion up to about 250,000 years ago, when (for reasons that remain a mystery) a sudden, explosive period of growth gave us a neocortex much larger and denser than that of any other species
- It can now be said that the human brain has decreased from 1,500 cubic centimeters (cc) to 1,350cc, irrespective of gender and race.
- We are headed on a path to have same-sized brain as Homo Erectus
- What will post 2020 bring ???

Increasing breadth of the frontal lobe but decreasing height of the human brain between two Chinese samples from a Neolithic site and from living humans " American Journal of Physical Anthropology 2014

UK Biobank study: Generalized Atrophy & Grey Matter Damage post COVID even in mild illness

From: SARS-CoV-2 is associated with changes in brain structure in UK Biobank

Top, the main analysis shows that the strongest, localized reductions in grey matter thickness in the 401 infected participants compared with the 384 controls are bilaterally in the parahippocampal gyrus, anterior cingulate cortex and temporal pole, as well as in the left orbitofrontal cortex, insula and supramarginal gyrus.

- Greater loss of grey matter in the lateral orbitofrontal cortex, the olfactory nucleus, para-hippocampal gyrus, anterior cingulate & temporal pole post COVID
- This volume loss translates to mental decline equivalent to 10 years of aging.
- Brain imaging before and after COVID-19 in UK Biobank Soojin, G et al Bmj Yale October 2021

For millions of years the hominid brain has grown increasingly bigger. But for the last 10,000 years, the human brain has been shrinking at an alarming rate and no one really knows why.

Severe COVID-19 is associated with molecular signatures of aging in the human brain Mavrikaki M et al Nature Aging Dec 5 2022 Those who died from COVID had molecular signatures of advanced aging

Gene expression in the brain tissue of patients who died of COVID-19 closely resembled that of uninfected individuals 71 years old or older

High levels of DNA damage, mitochondrial function, oxidative stress, vesicular transport, calcium homeostasis, neuroinflammation, TNF and Type I/II interferon but NO VIRUS

SARS COV 2 with its long-term complications including advanced senescence will lead to premature aging (in terms of health) of many people in the world (Tayeri K 2022)

Shrinking Teenage Brains

- A small study comparing brain scans of young people from before and after 2020 reveals that the brains of teens who lived through the pandemic look about three years older than expected
- Adolescents assessed during the pandemic showed signs of advanced cortical thinning and had larger bilateral hippocampal and amygdala volumes
- Our Youth experience a tremendous fall out to their emotional health as a result of the pandemic counter measures

Effects of the COVID-19 Pandemic on Mental Health and Brain Maturation in Adolescents: Implications for Analyzing Longitudinal Data Gotib I et al Biological Psychiatry Dec 2022

Cortical Gray Matter Loss in Long COVID seen on NeuroQuant

- The results demonstrate a statistically significant depletion of CGM volume in 24 COVID-19 infected patients.
- Reduced CGM volume likely influences their long- term neurological sequelae and may impair post COVID-19 patient's quality of life and productivity.
- CGM contributes to memory, cognition, language, perception, movement, and emotions

Cortical Grey matter volume depletion links to neurological sequelae in post COVID-19 "long haulers" Rothstein T BMC Neurology

Accelerated Brain Volume Loss Caused by Anti– β -Amyloid Drugs: A Systematic Review and Meta-analysis Alves F et al Neurology 2023

Brain Structure	Volume (cm ³)	(5%-95% Normative Percentile)	Normative Percentile
Hippocampal Occupancy Score (HOC)	0.41	N/A	1
Hippocampi	4.52	0.25 (0.33 - 0.48)	1
Superior Lateral Ventricles	125.44	6.81 (1.88 - 5.25)	99
Inferior Lateral Ventricles	6.57	0.36 (0.15 - 0.31)	98
OF MARCHIER DEFENSION			

An example of NeuroQuant(@) numeric data acquisition and 3-dimensional voxel-based morphon results in patient \$7 is provided in Fig. 1 which tracks volumes of thalamus, hippocampus and co grey matter as their percentage of total intracranial volume (ICV) when compared with normativ latabase drawn from healthy controls and adjusted for age, and sex. Abnormal range is defined r seyond the white zone at the 5th percentile or less, or 95th percentile or more, at a given age

Fallout to the Brain will Result in Complex Neurological Problems for Years to Come

- No lingering virus but lingering spike protein
- Generalized neuroinflammation and activated microglia and in some multifocal encephalitis (Poli K 2023)
- High levels of glutamate (Yapir-Esser H 2023)
- Mitochondrial damage (Clough E 2021)
- Damage to the hippocampus and other critical cognitive centers and volume loss (especially to gray matter (Rothstein T 2023)
- Damage to the cells lining the brain's blood vessels, clotting and vascular inflammation (vasculitis) (Ramdani Y 2022)
- Molecular Mimicry and autoantibodies (Vorjdani 2021)
- Dying neurons (Crunfii F 2021) (Planton D 2022)
- Prions fueled (Nystrom S 2022)
- Alteration of the Acetylcholine nicotinic receptors (Rivas M 2022)
- May change genetic expression (Alden M 2022)

Nervous system consequences of COVID-19 Science Spudich S & Nath A Jan 2022

Unless All Of Us Resist, Never Again Is Now"

Vera Sharav

