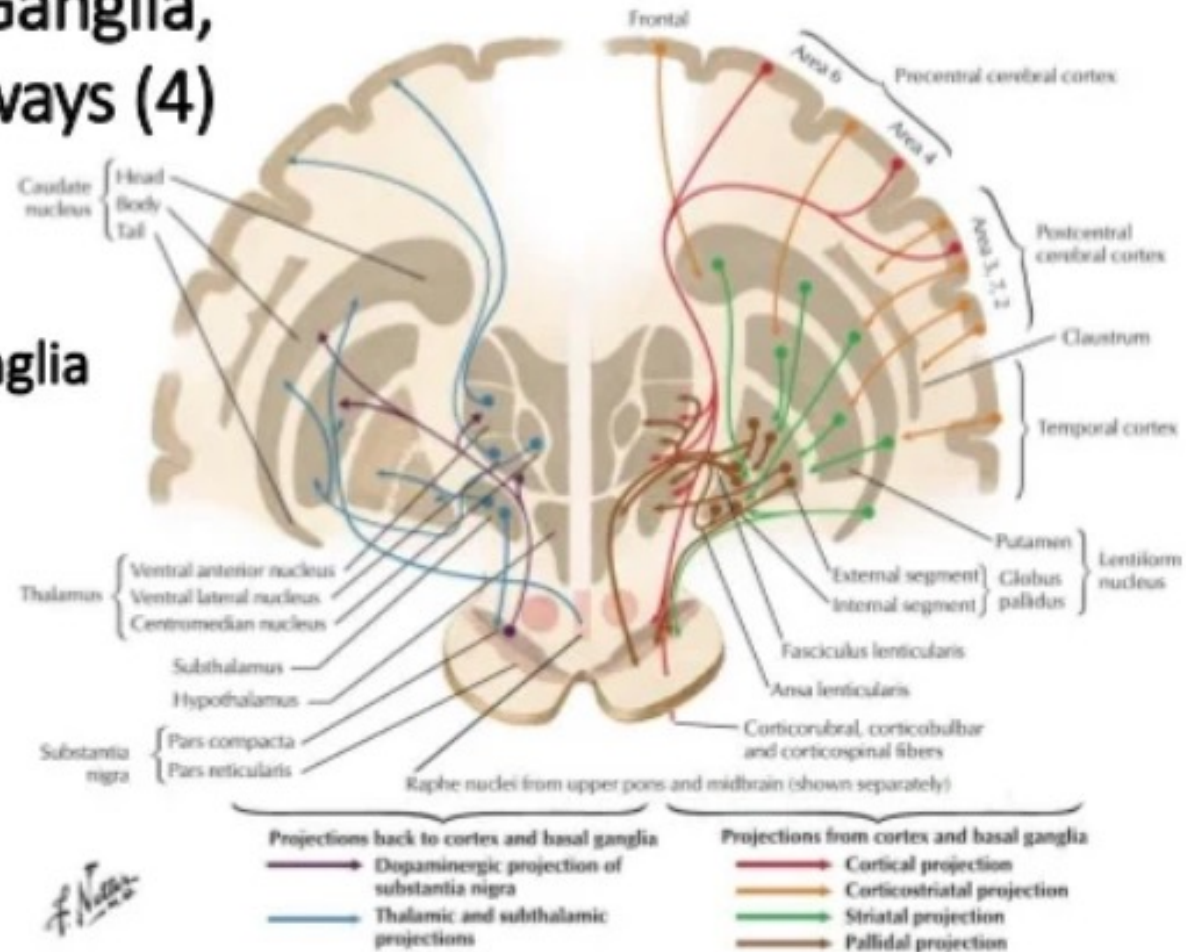


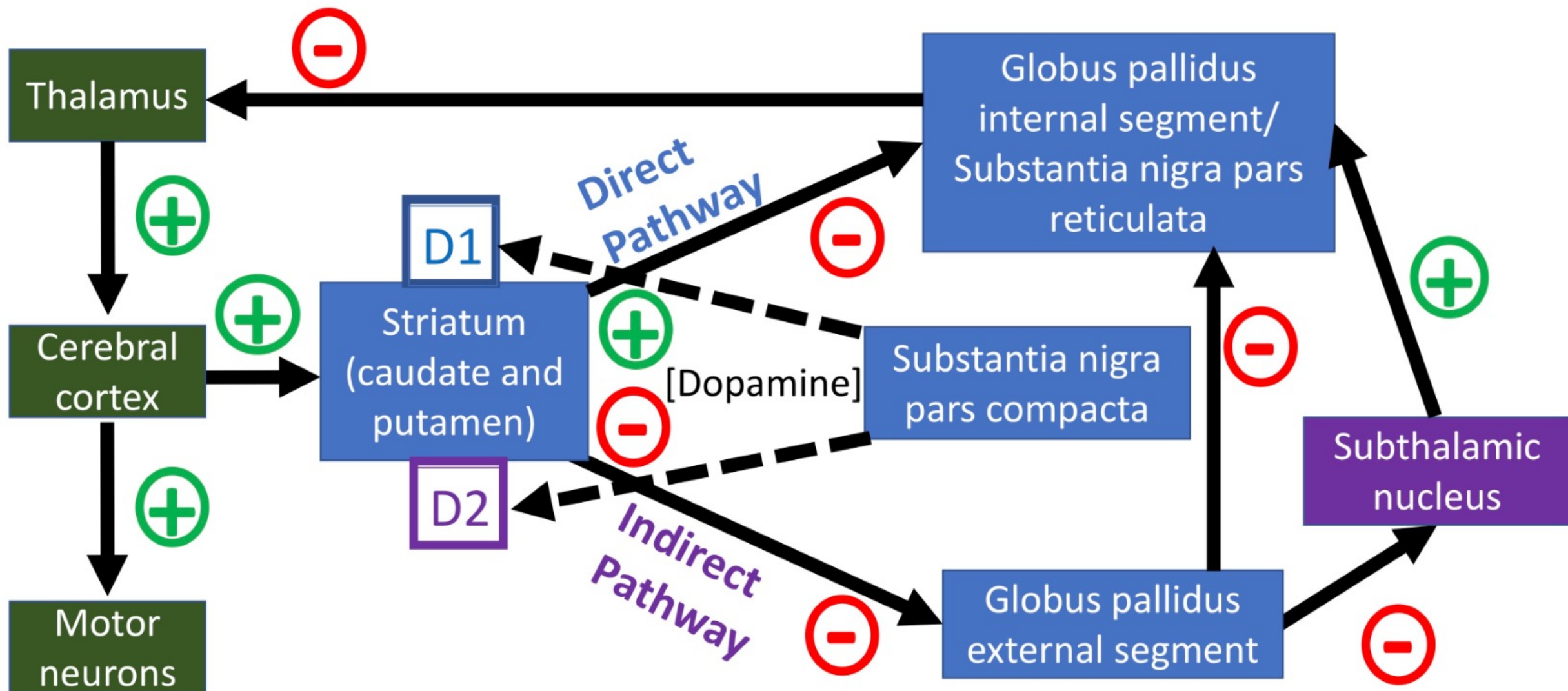
SPIKE PROTEIN induced MOVEMENT DISORDERS



Motor Tracts, Basal Ganglia, and Dopamine Pathways (4)

Connections of Basal Ganglia





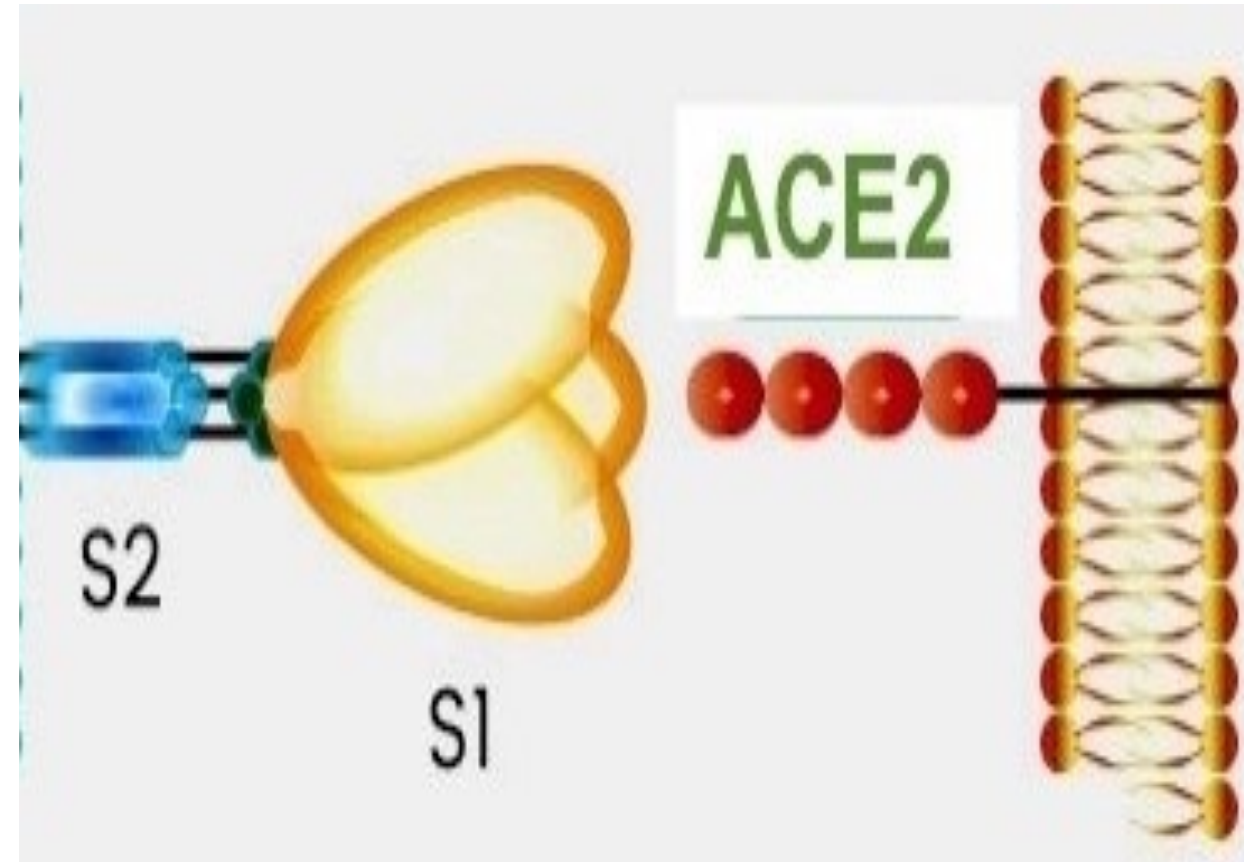
BASIC PREMISES:

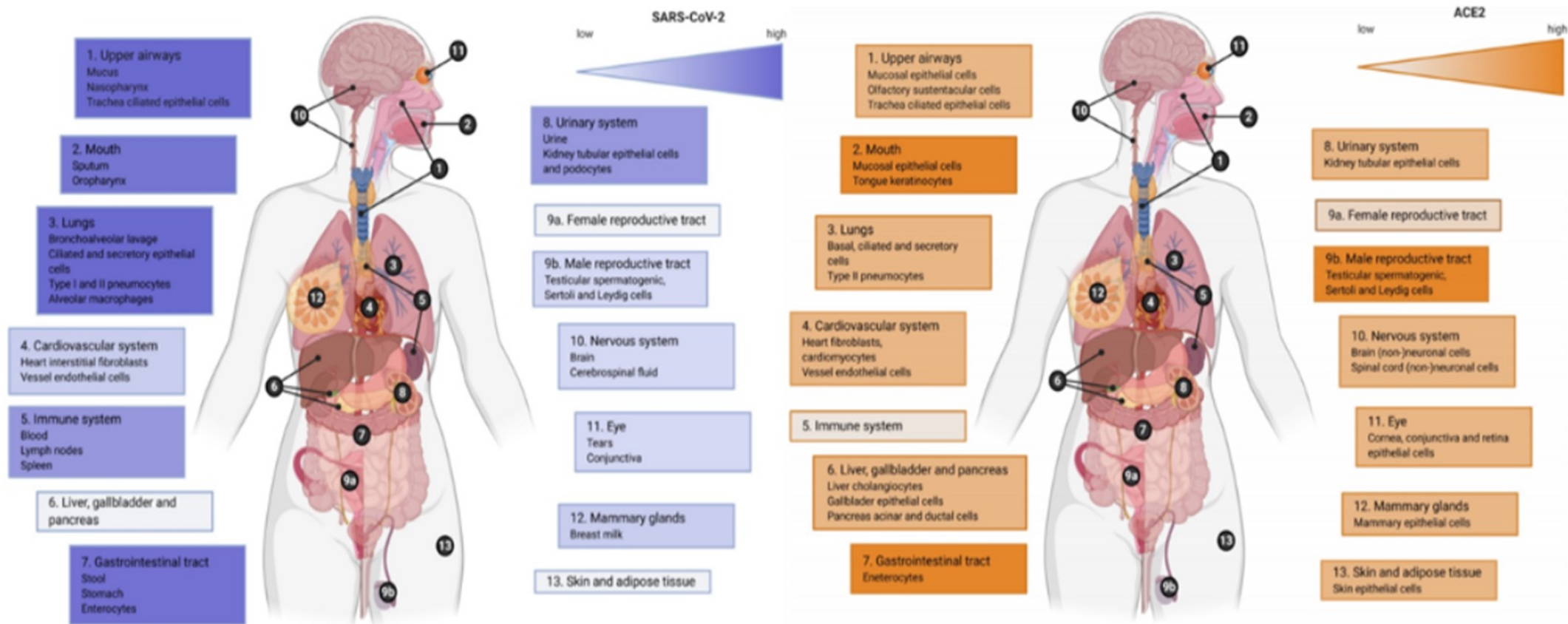
Spike Protein- S1 and S2 subunits

ACE 2 receptors- Primary cellular binding target

Additional receptors (TLR4) and proteins, (TMPRSS2 and P2X7), are involved

ACE 2 receptors- upregulated in HTN, DM, smokers, and dementia

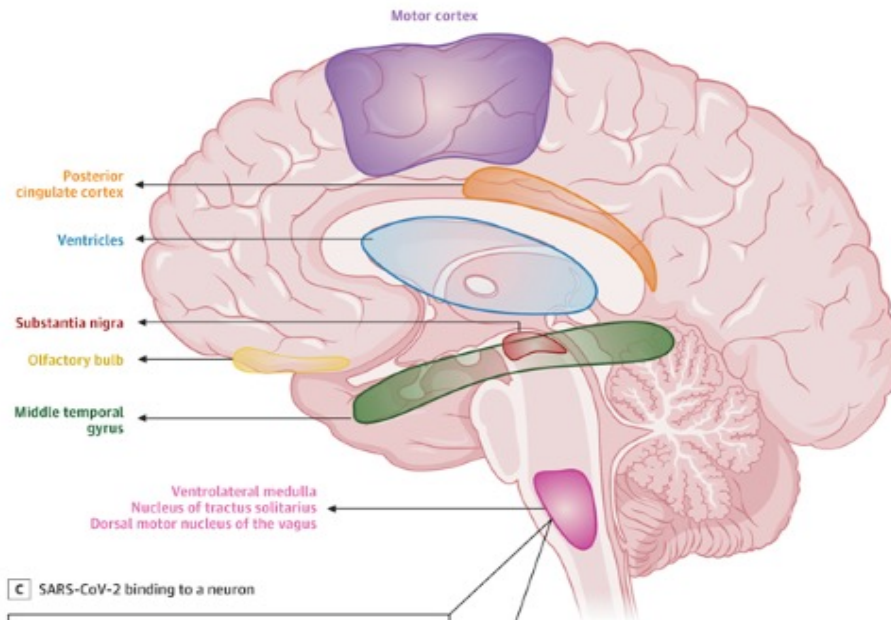




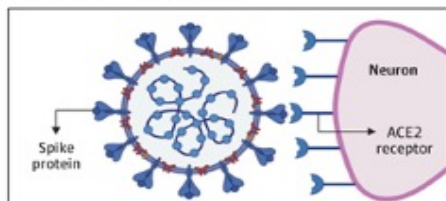
Trypsteen et al. (2020). Left: Gradient color (purple) indicates low to high evidence for SARS-CoV-2 detection; the highest expression was found in the upper airways, lungs, oral cavity, gastrointestinal tract, and urinary system. Right: Gradient color (orange) indicates low to high evidence for ACE2 expression; the highest expression was detected in the oral cavity, gastrointestinal tract, and the male reproductive system.

ACE 2 RECEPTORS in the BRAIN

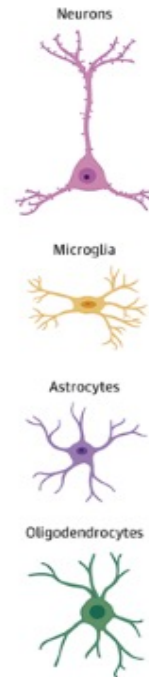
A Areas of the brain that express ACE2 receptors



C SARS-CoV-2 binding to a neuron



B Cell types that express ACE2 receptors in the central nervous system



- ▶ Choroid plexus
- ▶ Sympathetic pathways in the brainstem
- ▶ Different caliber of blood vessels: capillaries, arterioles, venules
- ▶ Pericytes
- ▶ Smooth muscle cells

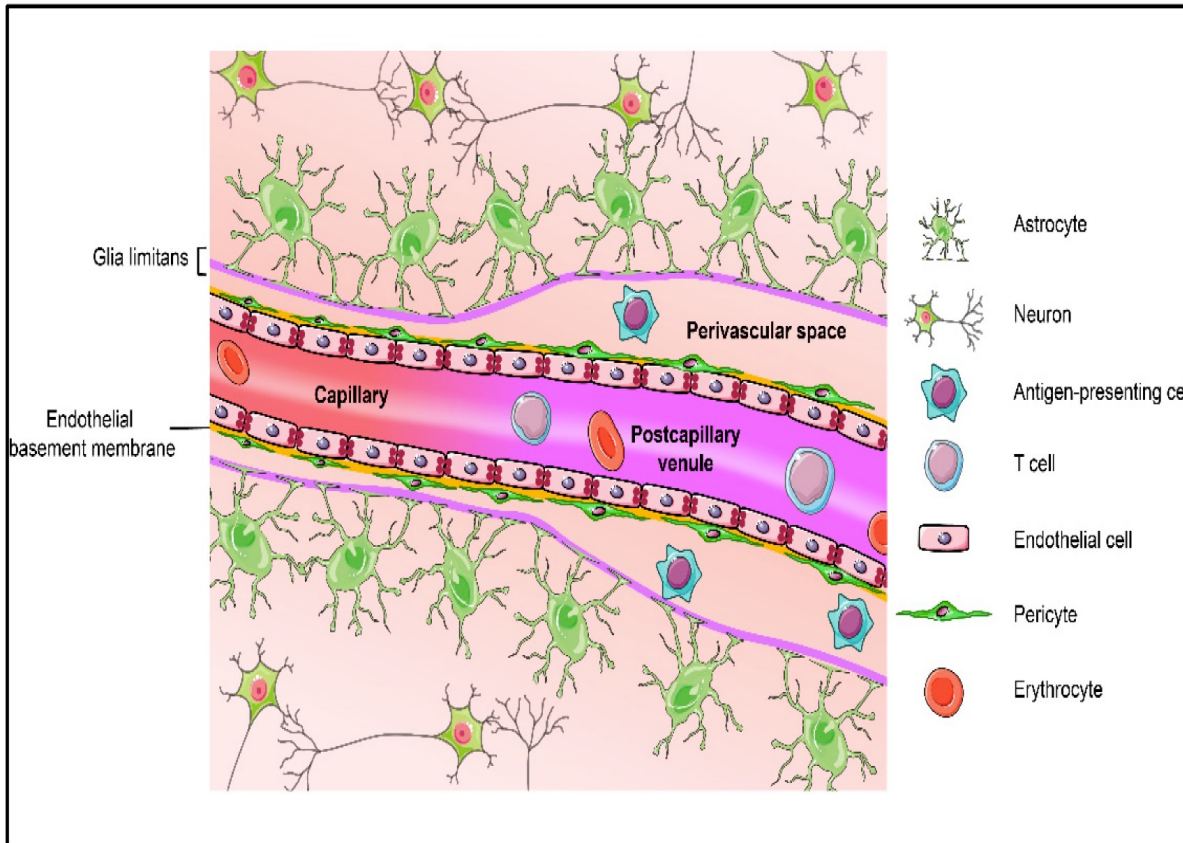
BLOOD BRAIN BARRIER

- BBB – a wall of highly dense cells that restrict the passage of substances from the blood to the brain
- Composed of vascular endothelium, astrocytes, pericytes, extracellular matrix
- ACE 2 receptors found on endothelium and pericytes

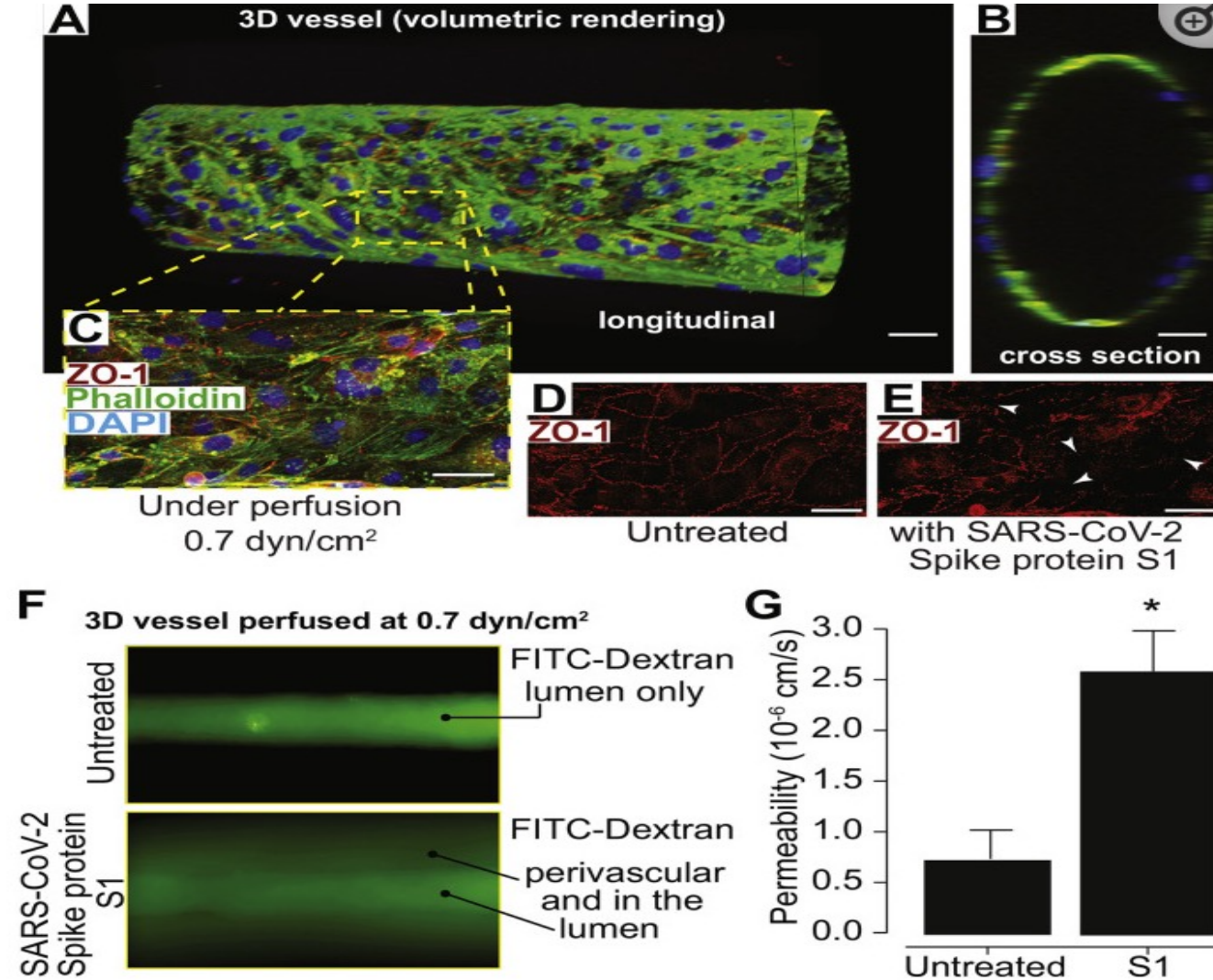


ENDOTHELIAL INJURY

mdpi.com/jms-20-05372/article_deploy/html/images/jms-20-05372-g001.png



- ▶ Damage to the endothelium causes inflammatory response with cytokines, chemokines, cell adhesion molecules
- ▶ Leads to further demise of structural and functional integrity of BBB
- ▶ Allows for free passage of particles and immune cells (Trojan horse) into the brain
- ▶ Increases inflammatory mediators
- ▶ Increases S1 uptake into the brain



SARS-CoV-2 subunit S1 alters barrier status in a 3D tissue engineered microfluidic model of the human BBB. Confocal microscopy and volumetric rendering were used to visualize the tissue engineered vessel. (A) Shows a longitudinal view of an endothelialized void after perfusion that formed a predictive vessel geometry analogous to those found within the brain. (B) provides a cross sectional perspective indicating a single layer of endothelial cells. In (C) a representative merged image of the engineered vessel constructs fixed and immunostained for the tight junction protein, ZO-1, along with phalloidin to label actin and the nuclear stain, DAPI. (D) shows the typical ZO-1 membranous pattern expected in mature barrier forming brain endothelial cells. (E) after perfusion for 2 h of SARS-CoV-2 subunit S1 (10 nM), constructs were also fixed and immunolabeled for ZO-1. The arrows point to areas in which the ZO-1 cellular pattern is discontinuous, punctate or absent signifying areas of barrier breach. Scalebar = 20 μ m. (F) Fluorescence intensity after ten minutes of perfusion with 4 kDa FITC-dextran, indicating the impaired barrier function in vessels perfused after 2 h of the S1 spike protein versus untreated controls. G) Quantitative measurements for permeability coefficients of vessels exposed to the SARS-CoV-2 subunit S1 compared to untreated controls. Data was analyzed using Kruskal-Willis test. $n = 3$. $*p < 0.05$.

ENDOTHELIAL INJURY

Biochemical Journal (2022) **479** 537–559
<https://doi.org/10.1042/BCJ20220016>



- ▶ Coagulopathy and microangiopathy arises
- ▶ Formation of fibrin amyloid microclots
- ▶ Resistant to fibrinolysis
- ▶ Leads to tissue damage, inflammation, autoantibodies
- ▶ Symptoms: SOB, fatigue, brain fog, CFS
- ▶ ? Vascular Parkinsonism and other abnormal movements

A central role for amyloid fibrin microclots in long COVID/PASC: origins and therapeutic implications; Douglas B. Kell, Gert Jacobus Laubscher, and Ethersia Pretorius

SARS-CoV-2 spike protein S1 induces fibrin(ogen) resistant to fibrinolysis: implications for microclot formation in COVID-19, Grobbelaar et al, Bioscience Reports 2021

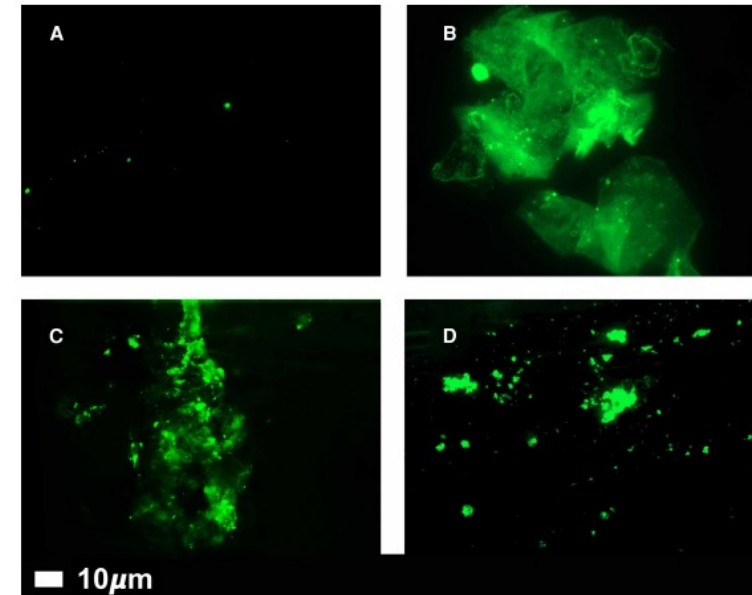


Figure 4. Fluorescence microscopy of representative micrographs showing microclots in the circulation of controls (A) and in patients with Long COVID (B–D).

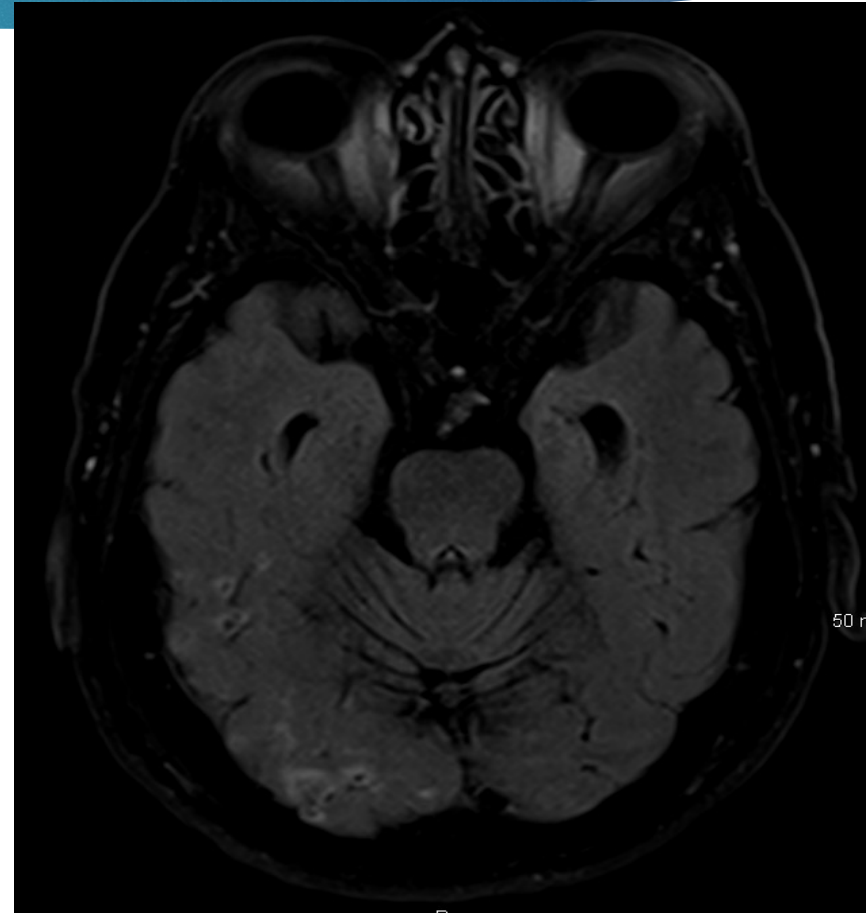
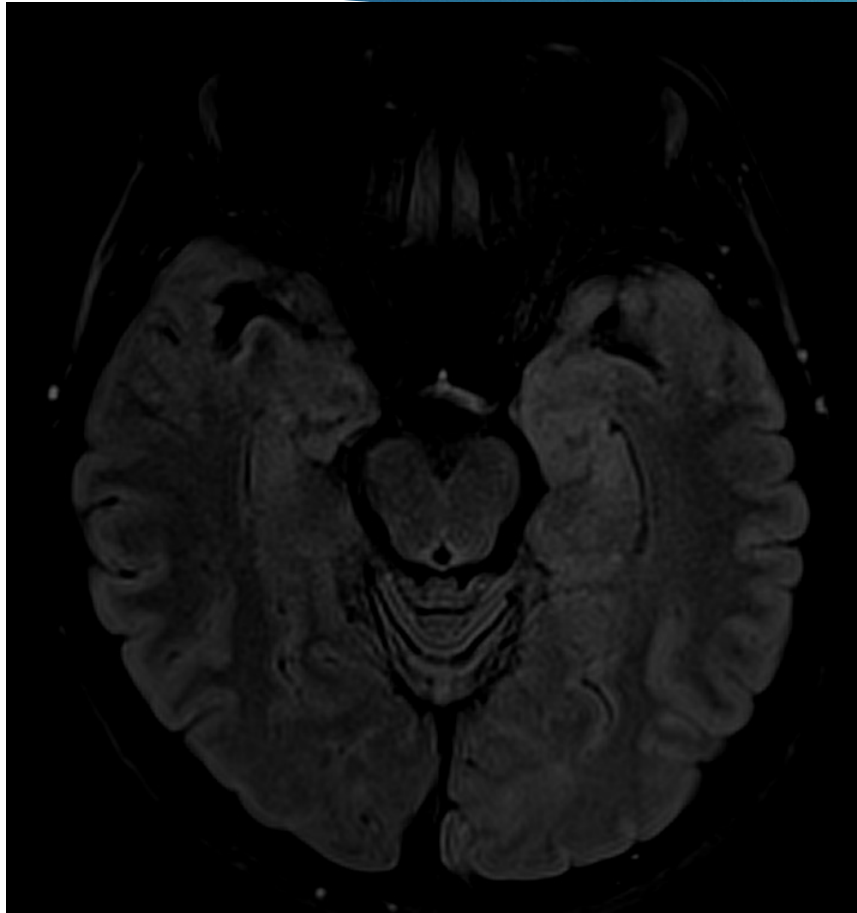
Absence of significant amyloid microclots in the plasma of 'normal' individuals, and their significant presence in the plasma of individuals with long COVID. Platelet-poor plasma was produced by centrifugation at 3000×g for 15 min, stained with 5 μM thioflavin T, and imaged in a fluorescence microscope (Zeiss Axio Observer 7 with a Plan-Apochromat 63×/1.4 Oil DIC M27 objective (Carl Zeiss Microscopy, Munich, Germany). Wavelengths were Exc 450–488 nm/emission 499–529 nm, all as in [108].

INFLAMMATION



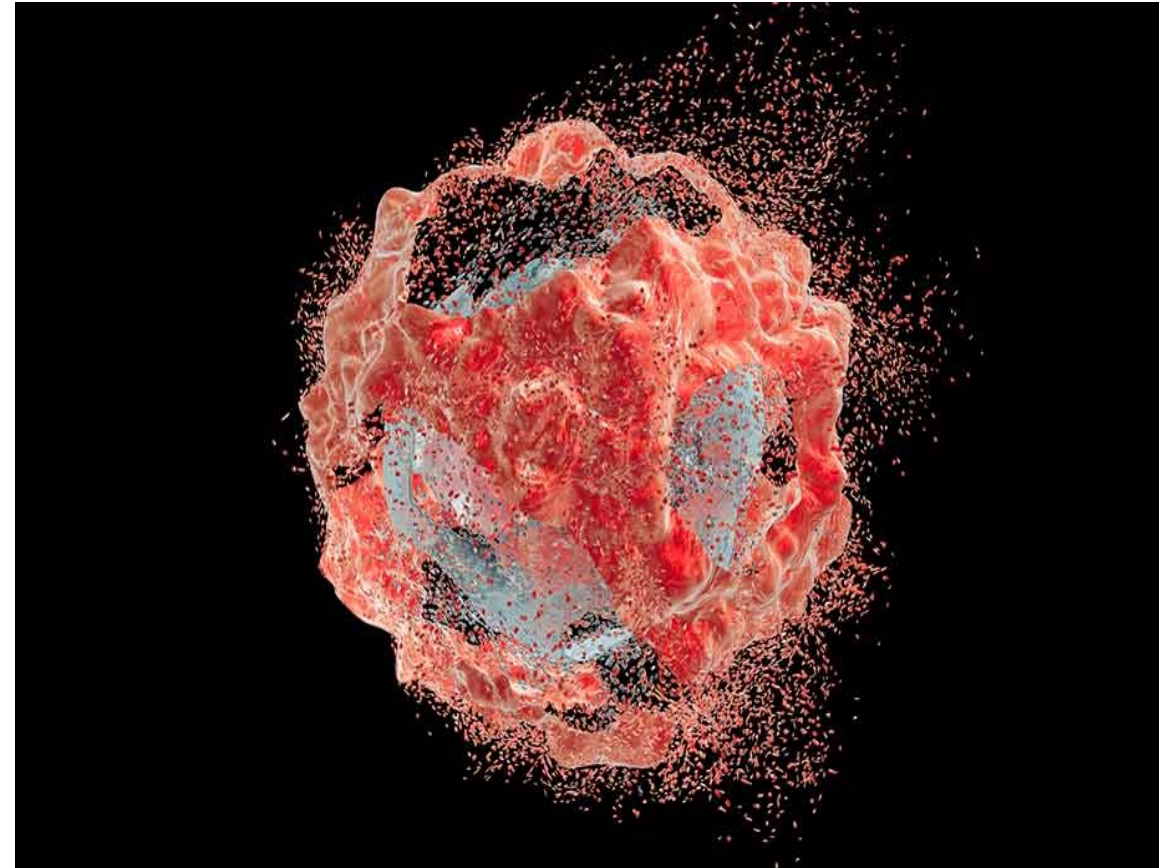
- ▶ Neuro-inflammation and cytokine release (prior to or along with development of antibodies previously discussed)
- ▶ Especially TNF alpha
- ▶ Impaired function of dopaminergic receptors
- ▶ Directly promotes neurodegeneration (activates microglia and increases further inflammation)
- ▶ Inflammation allows for increased uptake of S1 in the brain

LEFT: 41 y/o male, military intel
RIGHT: 80 y/o male, lawyer



DIRECT HIT and INVASION

- ▶ Spike protein can bind to ACE 2 receptors and cause neuronal death
- ▶ Neurons take up the mRNA and express spike protein on their surface, triggering cytotoxic T cell attacks
- ▶ Exosomes traveling via Vagus Nerve
- ▶ Neurons do not regenerate
- ▶ Amyloid formation with prion-like spread
- ▶ CSF biomarkers: NfL (neurofilament light chain protein), GFAP (glial fibrillary acid protein), T tau, P tau

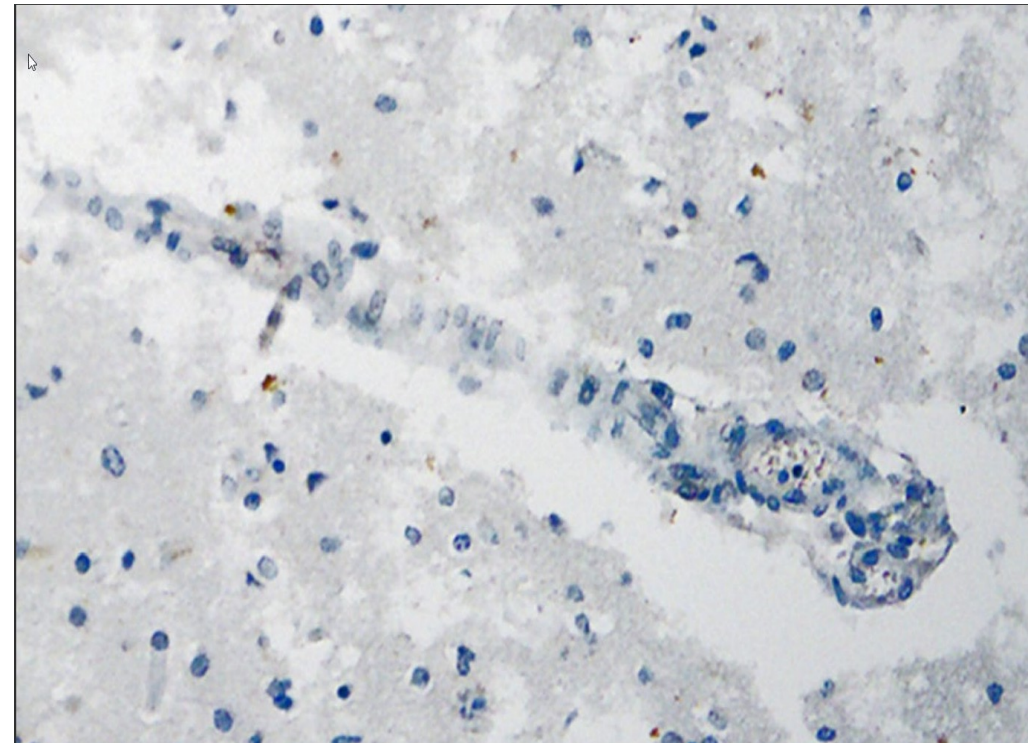
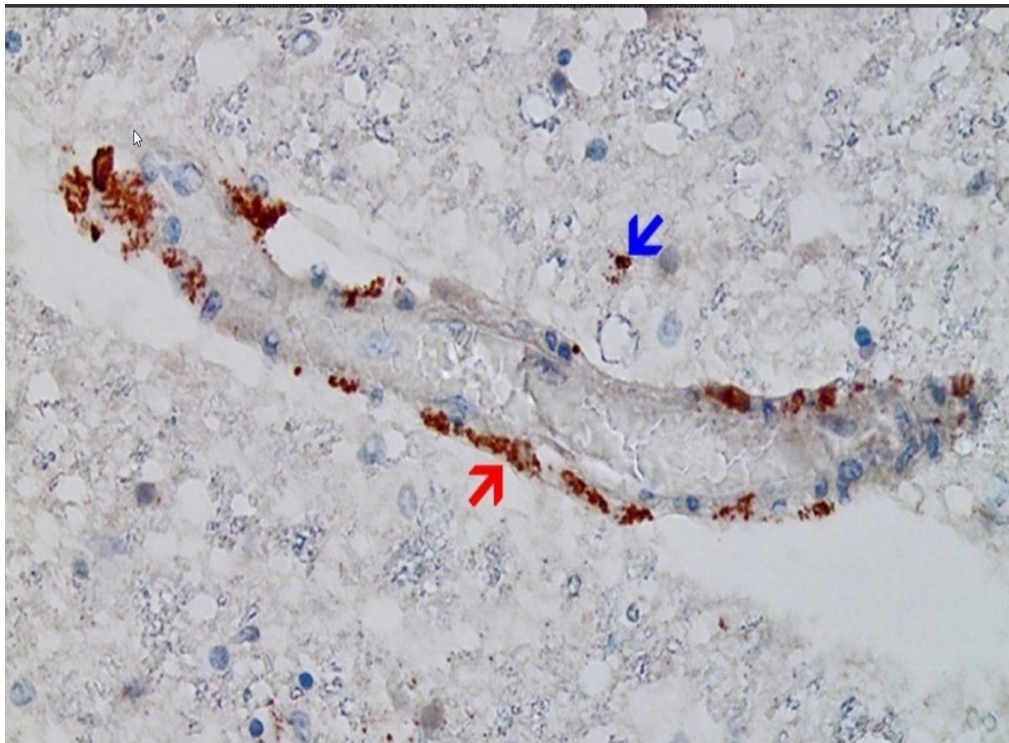


Pfizer mRNA Spike Protein Found in Deceased Man's Brain and Heart: Peer-Reviewed Report ([Kanekoa News](#) Oct 2, 2022)

- Had worsening of his baseline Parkinson's, requiring a wheelchair, and developed lethargy, anxiety, social withdrawal after Pfizer 7/21 (Astra Zeneca 5/21)
- 2 weeks after Pfizer 12/21, he collapsed x 2 in 3 week period and died shortly after

LEFT: stain for SARS-CoV-2 spike protein in swollen endothelium of a capillary vessel and glial cells

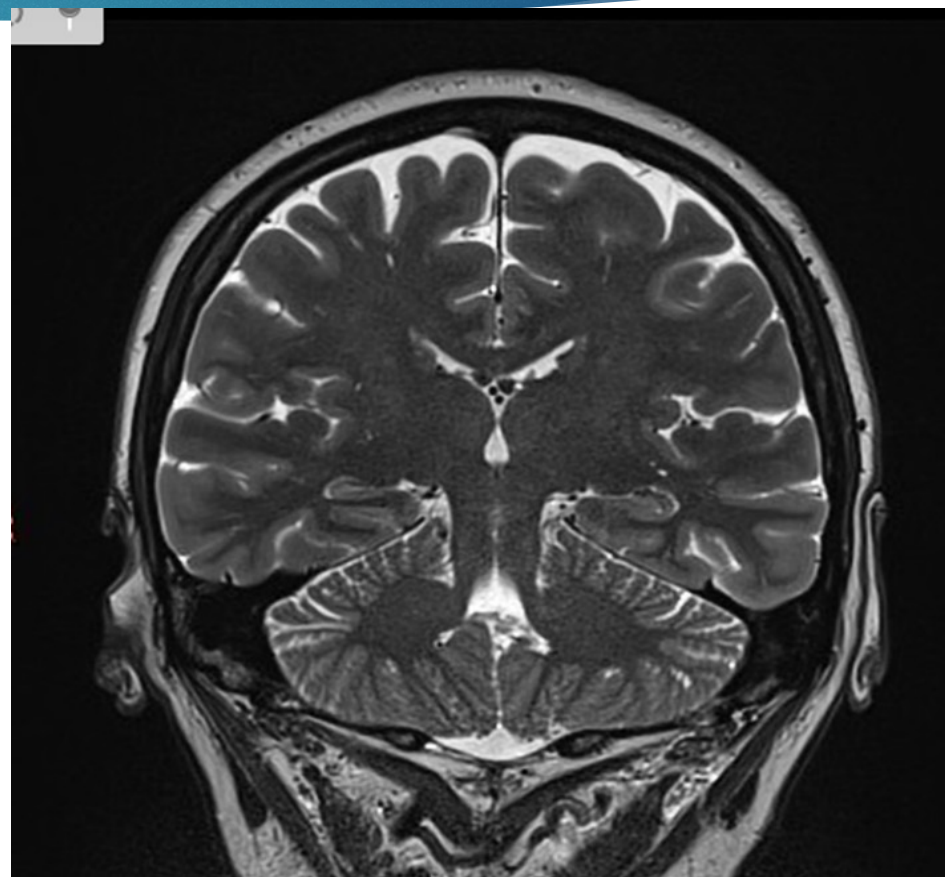
RIGHT: negative stain for nucleocapsid protein (virus)



STRUCTURAL BRAIN CHANGES

- ▶ Reduction of gray matter thickness
- ▶ Reduction of global brain size
- ▶ CT changes: capsulogangliomic and thalamic infarcts with hemorrhagic transformation of the left thalamus
- ▶ MRI changes:
 - ▶ Bilateral hyperintensities of basal ganglia
 - ▶ Diffuse white matter hyperintensities
 - ▶ Cortical and subcortical atrophy
 - ▶ Hypointense signal of dorsolateral bilateral putamen
 - ▶ Leptomeningeal enhancement
 - ▶ Frontotemporal hypoperfusion
 - ▶ Alterations of nigrosomes (substantia nigra)

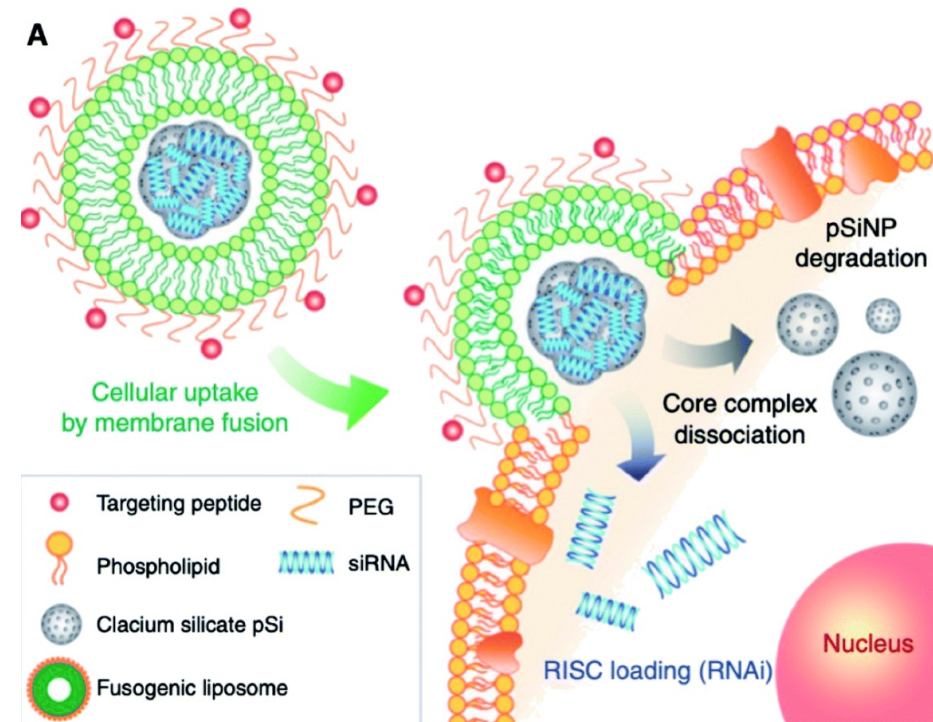
LEFT: 47 y/o vaccine injured female
RIGHT: NORMAL stock photo age 48




WHAT ELSE..... Lipid Nanoparticles?

- ▶ Little has been reported on the tissue localization of the LNPs used
- ▶ Dr. Jessica Rose reported with the Ask Dr. Drew show Feb 2023:
- ▶ Moderna uses LNP SM-102 that has not been approved in animals or humans, only in the lab
- ▶ “Pronounced changes in both clot morphology and kinetics of fibrin clotting in the presence of artificial liposomes.... accelerates fibrin polymerization”


Direct interaction of fibrinogen with lipid microparticles modulates clotting kinetics and clot structure, Dzhigangir et al, Nanomedicine 2020 Jan;23:102098



Species (Strain):	Rat (Wistar Han)
Sex / Number of Animals:	Male and female / 3 animals / sex / timepoint (21 animals / sex total for the 50 µg dose)
Feeding Condition:	Fed ad libitum
Method of Administration:	Intramuscular injection
Dose:	50 µg [3 H] -08-A01-C0 (lot # NC-0552-1)
Number of Doses:	1
Detection:	Radioactivity quantitation using liquid scintillation counting
Sampling Time (hour):	0.25, 1, 2, 4, 8, 24, and 48 hours post-injection



Sample	Mean total lipid concentration (µg lipid equivalent / g (or mL)) (males and females combined)							% of administered dose (males and females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Adipose tissue	0.057	0.100	0.126	0.128	0.093	0.084	0.181	-	-	-	-	-	-	-
Adrenal glands	0.271	1.48	2.72	2.89	6.80	13.8	18.2	0.001	0.007	0.010	0.015	0.035	0.066	0.106
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365	0.000	0.001	0.001	0.001	0.001	0.002	0.002
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687	-	-	-	-	-	-	-
Bone marrow (femur)	0.479	0.960	1.24	1.24	1.84	2.49	3.77	-	-	-	-	-	-	-
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068	0.007	0.013	0.020	0.016	0.011	0.010	0.009
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112	0.000	0.001	0.001	0.002	0.002	0.002	0.003
Heart	0.282	1.03	1.40	0.987	0.790	0.451	0.546	0.018	0.056	0.084	0.060	0.042	0.027	0.030
Injection site	128	394	311	338	213	195	165	19.9	52.6	31.6	28.4	21.9	29.1	24.6
Kidneys	0.391	1.16	2.05	0.924	0.590	0.426	0.425	0.050	0.124	0.211	0.109	0.075	0.054	0.057
Large intestine	0.013	0.048	0.093	0.287	0.649	1.10	1.34	0.008	0.025	0.065	0.192	0.405	0.692	0.762
Liver	0.737	4.63	11.0	16.5	26.5	19.2	24.3	0.602	2.87	7.33	11.9	18.1	15.4	16.2
Lung	0.492	1.21	1.83	1.50	1.15	1.04	1.09	0.052	0.101	0.178	0.169	0.122	0.101	0.101

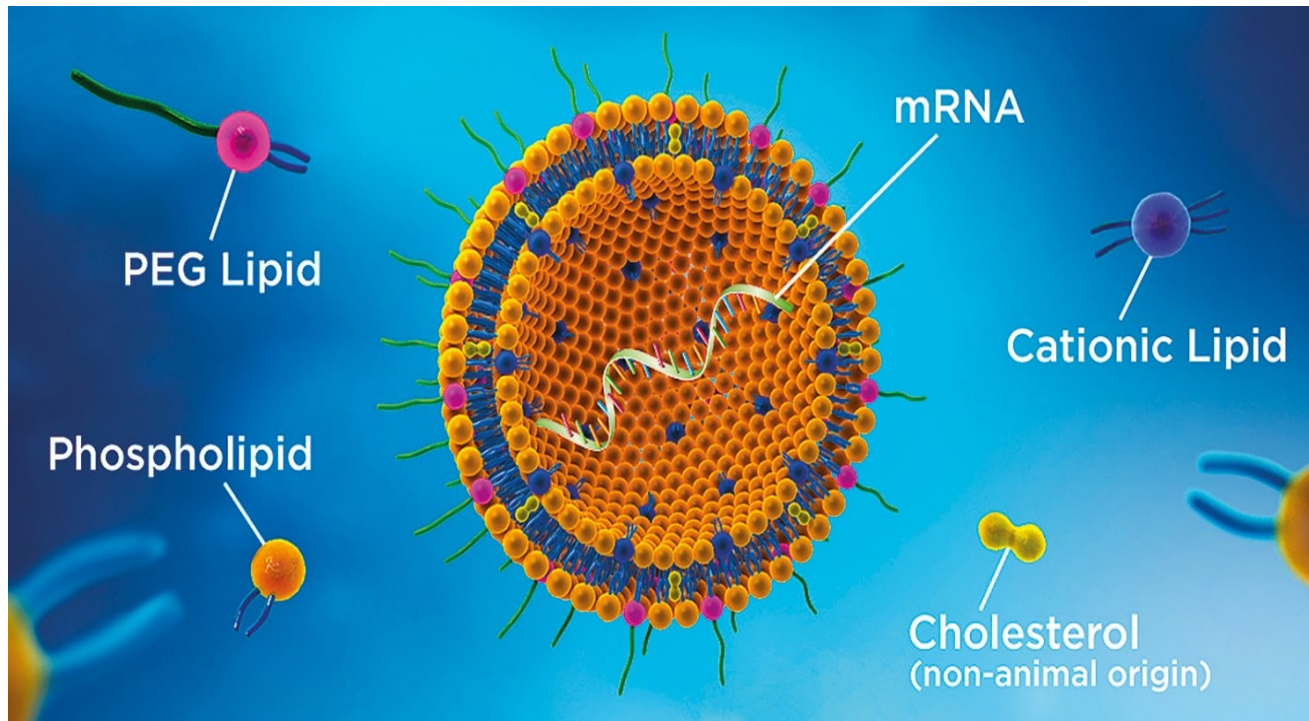


**2.6.5.5B. PHARMACOKINETICS: ORGAN
DISTRIBUTION CONTINUED**

**Test Article: [3 H]-Labelled LNP-mRNA formulation containing
ALC-0315 and ALC-0159
Report Number: 185350**

Sample	Total Lipid concentration (µg lipid equivalent / g [or mL]) (males and females combined)							% of Administered Dose (males and females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Lymph node (mandibular)	0.064	0.189	0.290	0.408	0.534	0.554	0.727	-	-	-	-	-	-	-
Lymph node (mesenteric)	0.050	0.146	0.530	0.489	0.689	0.985	1.37	-	-	-	-	-	-	-
Muscle	0.021	0.061	0.084	0.103	0.096	0.095	0.192	-	-	-	-	-	-	-
Ovaries (females)	0.104	1.34	1.64	2.34	3.09	5.24	12.3	0.001	0.009	0.008	0.016	0.025	0.037	0.095
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599	0.003	0.007	0.014	0.015	0.015	0.011	0.019
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694	0.000	0.001	0.001	0.001	0.000	0.000	0.001
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170	0.001	0.001	0.002	0.003	0.003	0.004	0.003
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264	0.003	0.007	0.008	0.008	0.005	0.006	0.009
Skin	0.013	0.208	0.159	0.145	0.119	0.157	0.253	-	-	-	-	-	-	-
Small intestine	0.030	0.221	0.476	0.879	1.28	1.30	1.47	0.024	0.130	0.319	0.543	0.776	0.906	0.835
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112	0.001	0.002	0.002	0.003	0.001	0.001	0.001
Spleen	0.334	2.47	7.73	10.3	22.1	20.1	23.4	0.013	0.093	0.325	0.385	0.982	0.821	1.03
Stomach	0.017	0.065	0.115	0.144	0.268	0.152	0.215	0.006	0.019	0.034	0.030	0.040	0.037	0.039
Testes (males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320	0.007	0.010	0.017	0.030	0.034	0.074	0.074
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331	0.004	0.007	0.010	0.012	0.008	0.007	0.008
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.00	0.000	0.001	0.001	0.001	0.001	0.001	0.001
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.456	0.002	0.011	0.015	0.008	0.016	0.018	0.022
Whole blood	1.97	4.37	5.40	3.05	1.31	0.909	0.420	-	-	-	-	-	-	-
Plasma	3.97	8.13	8.90	6.50	2.36	1.78	0.805	-	-	-	-	-	-	-
Blood: Plasma ratio a	0.815	0.515	0.550	0.510	0.555	0.530	0.540	-	-	-	-	-	-	-

WHAT ELSE.....PEG?



- ▶ Polyethylene glycol (PEG) is derived from the by-products produced during the refinement of petroleum, natural gas, or coal.
- ▶ The compounds polyethylene and glycol have been bonded together.
- ▶ Different forms are delineated by placing a number after the abbreviation "PEG," such as PEG-100, PEG-3350, etc, to denote molecular weight
- ▶ PEG is *hydrophilic* – meaning they dissolve in water and tend to attract water.
- ▶ Used for electrical neutrality, decreasing protein adherence and macrophage removal, extending half-life of the product

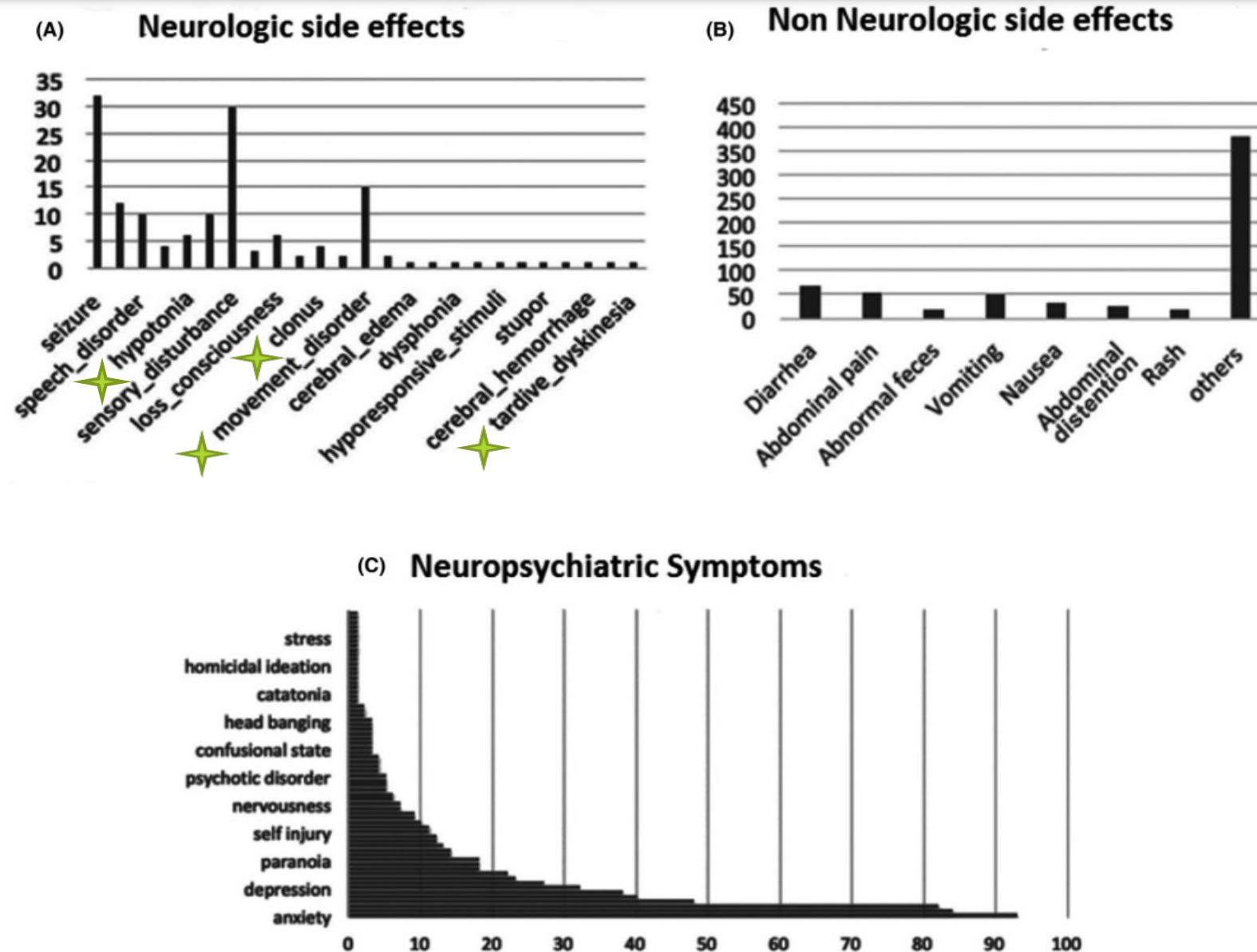


FIGURE 1 Adverse Effects of PEG 3350. A, Neurologic side effects. As reported in the Federal Drug Administration (FDA) Adverse Reporting System (AERS) data. B, Non Neurologic side effects. As reported in the Federal Drug Administration (FDA) Adverse Reporting System (AERS) data. C, Neuropsychiatric side effects. As reported in the Federal Drug Administration (FDA) Adverse Reporting System (AERS) data

Patient Case #1

62 YEAR OLD MALE

- ▶ COVID Spring 2020, Moderna 1/1/21, 1/29/21, 9/17/21
- ▶ Symptoms started 7/21: face would move involuntarily when he would read (Meigs's), then developed eyelid apraxia (blepharospasm), then his head began to turn to the right (CD)
- ▶ Mouth makes smacking motion, says "ahhh" or coughs before movements
- ▶ Lights and reading makes movements worse
- ▶ MRI Head- normal
- ▶ Eval included: DRD, Wilson's, PKD, RMSF, NMDA ab, paraneoplastic, AchR Ab
- ▶ Seen by UAB 2/22 (Dx'd with FND) and then Mayo 11/22
- ▶ Not responsive to FLCCC protocol 10/21 OR EMG guided Xeomin up to 380 units (x3), great response to Benadryl which decreased over time
- ▶ 5/22 c/o dizziness: ANS showed small fiber neuropathy and dysautonomia

Patient Case #2

34 YEAR OLD Special OPS Helicopter Pilot (Army x 16 yrs)

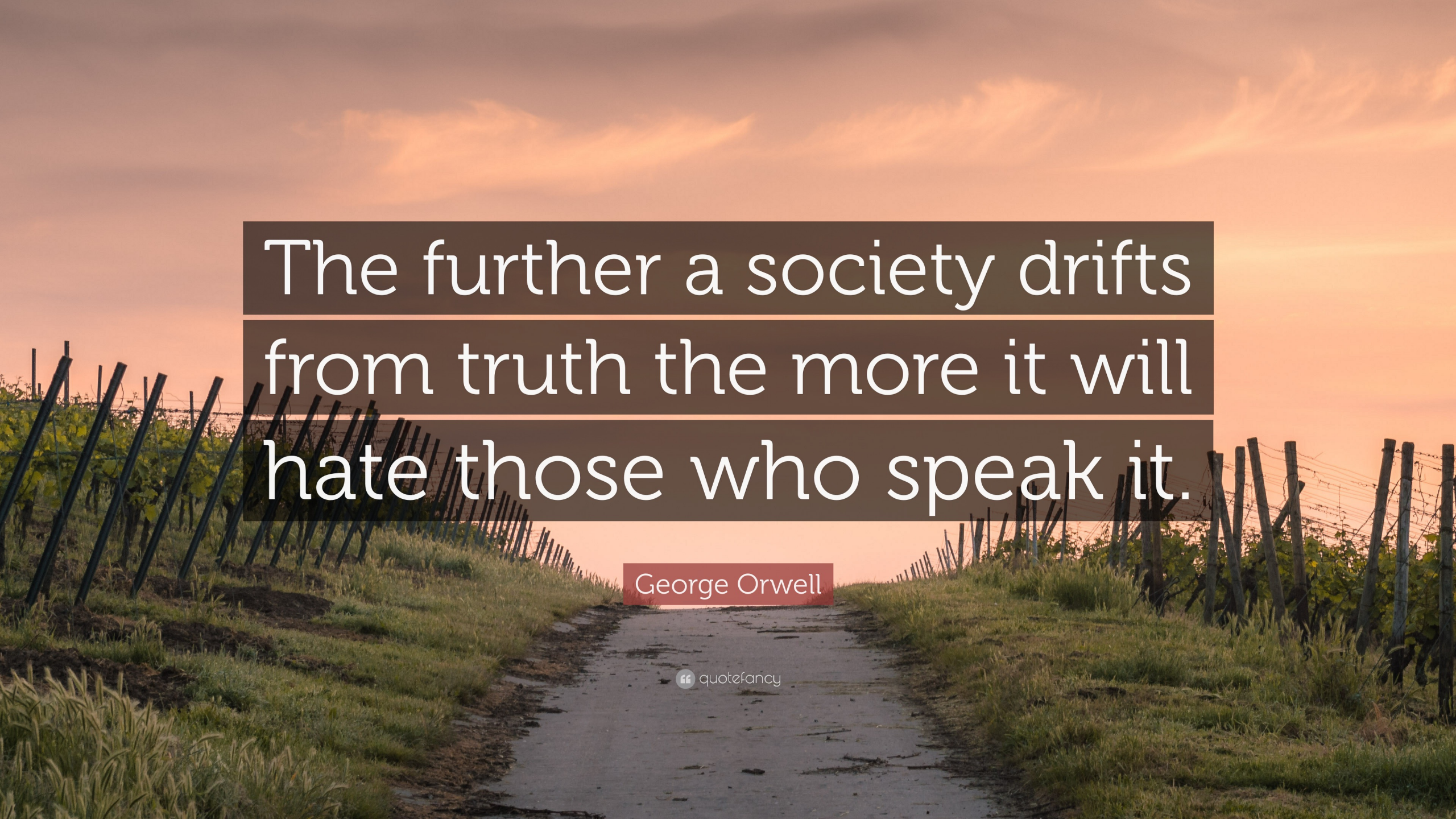
- ▶ Pfizer vaccine 3/21 and 4/21 in TN, sick for 1-2 days, weakness left arm
- ▶ Continued to get viruses, bronchitis afterwards (unusual for him); wife's menstrual cycle became abnl (but not vaxxed)
- ▶ COVID 2/22 with 2 weeks of symptoms
- ▶ Starting 3/22: Has, dizziness, fatigue, brain fog, face pulling to right, right shoulder and neck contraction to right (CD), stuttering, LBP, elevated BP (145/90), constipation, constant blinking (bleph), stiffness (hard to turn in bed), increase urination and urgency, altered smell, micrographia, RLS, heart palpitations, weight gain, right occipital neuralgia, right thumb rest tremor, hypophonia, change in demeanor, spastic gait on right (foot flexed and inward, toes flexed)

Patient Case #2

- ▶ Dat Scan, MRI Head, MRI LS spine- NORMAL
- ▶ Army physicians (x2) diagnosed with Somatoform disorder (FND)
- ▶ My diagnoses:
 - ▶ Parkinson's
 - ▶ RLS
 - ▶ Peripheral neuropathy
 - ▶ Cervical dystonia
 - ▶ Resolved blepharospasm
 - ▶ Right leg spasticity
 - ▶ Migraine
 - ▶ Right occipital neuralgia

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A photograph of a dirt road winding through a vineyard at sunset. The road is muddy and reflects the orange light of the sky. The vineyard rows are visible on both sides, with wooden posts and wires supporting the vines. The sky is a mix of orange, pink, and grey clouds.

The further a society drifts
from truth the more it will
hate those who speak it.

George Orwell