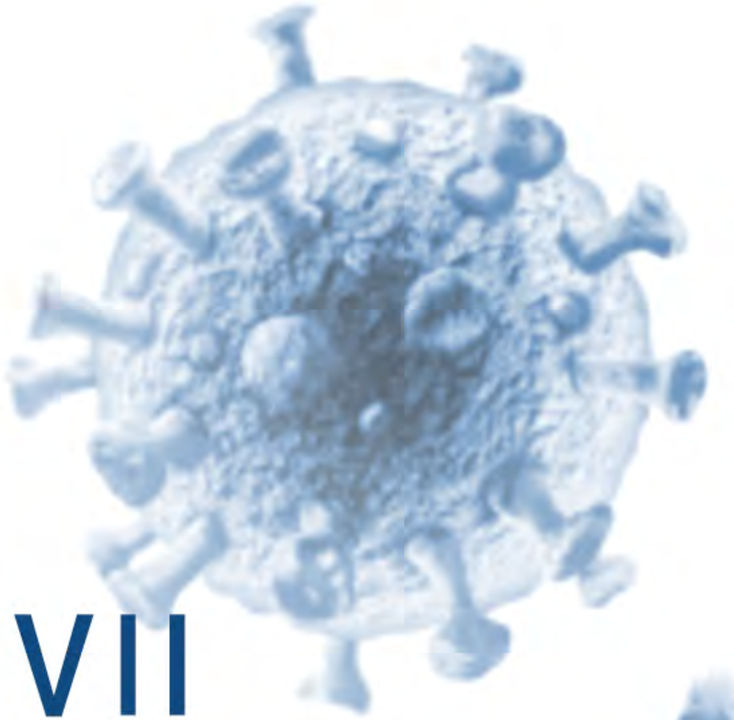
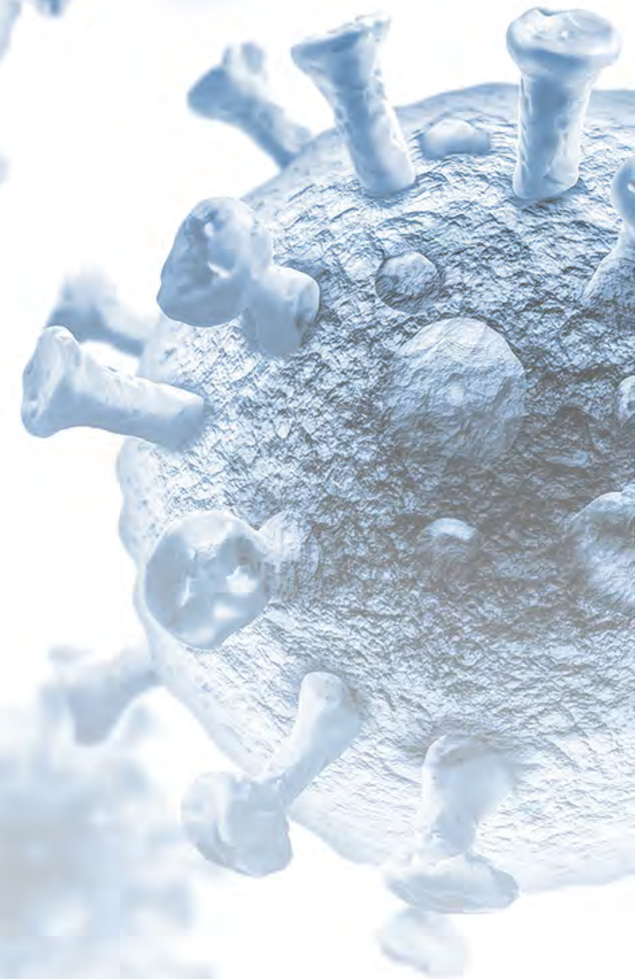
Welcome to the Front Lines
of the Fight Against COVID-19

A TOWN HALL CONVERSATION VII

We will begin at 10 a.m.

HOUSTON Methodist®
LEADING MEDICINE

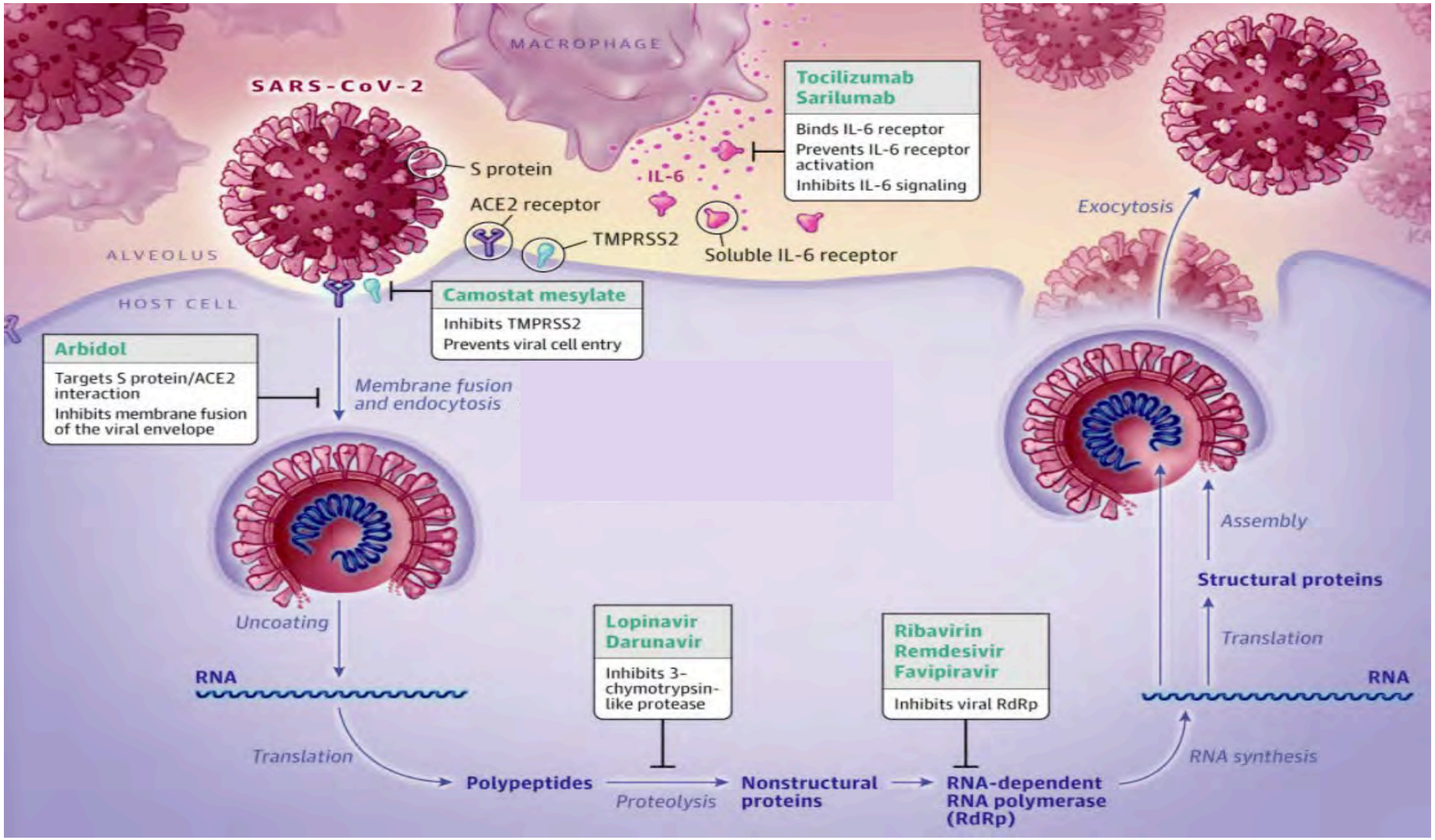




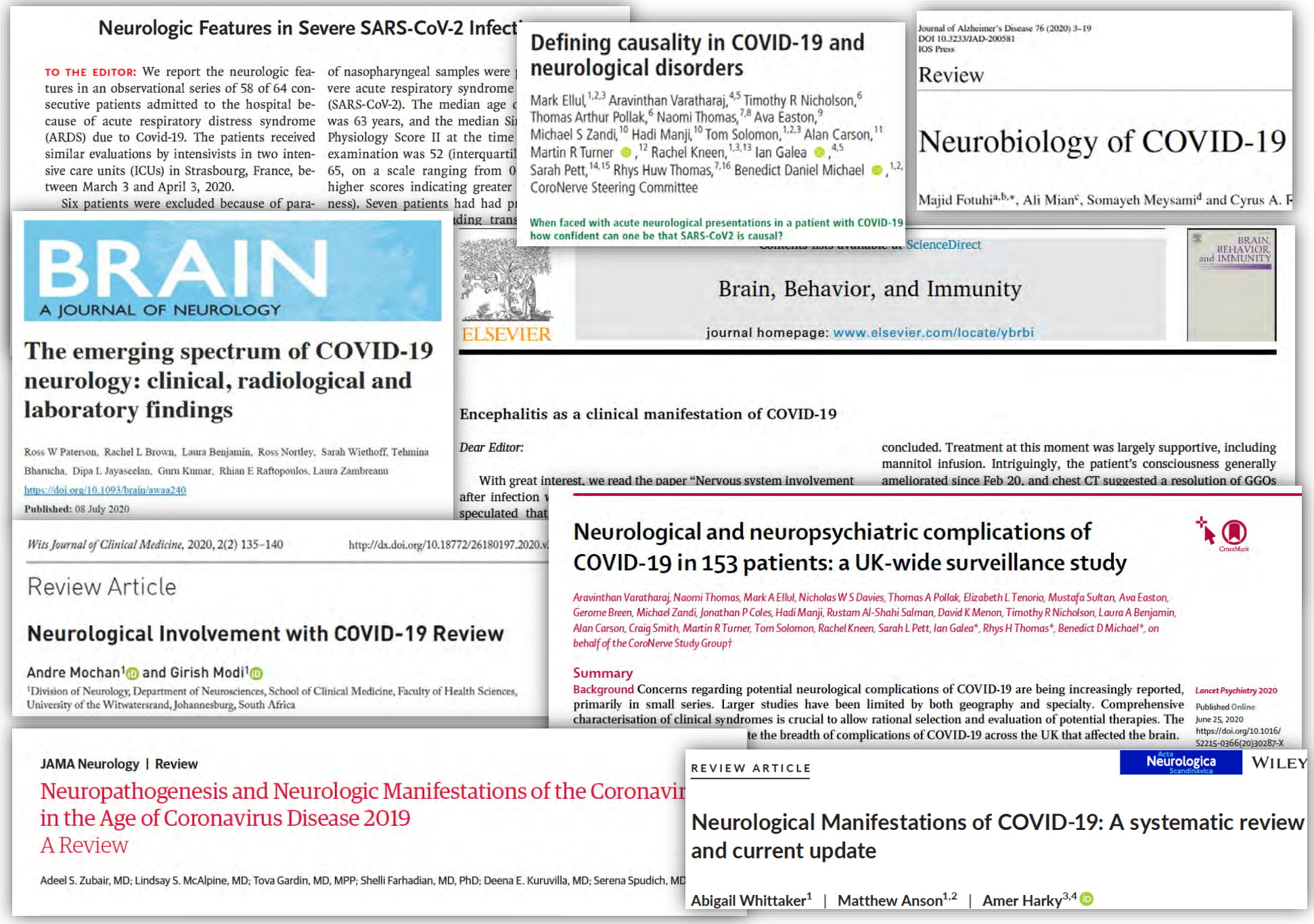
Clinical Manifestations

- Acute respiratory distress syndrome (ARDS)
- Hyper-inflammation (“cytokine storm”)
- Acute cardiac injury, arrhythmias, cardiomyopathy
- Acute kidney injury
- Hypercoagulability, thromboembolic complications, pulmonary embolism
- Neurological complications

Disease Pathogenesis - SARS-COV-2



The viral spike protein uses the angiotensin-converting enzyme II (ACE2) receptor to enter epithelial cells. Alveolar cells lining lungs, GI tract, heart and kidney express ACE2 R and membrane TMPRSS2 serine protease cleave the viral spike protein and facilitate cell entry.



Neurologic Features in Severe SARS-CoV-2 Infect

TO THE EDITOR: We report the neurologic features in an observational series of 58 of 64 consecutive patients admitted to the hospital because of acute respiratory distress syndrome (ARDS) due to Covid-19. The patients received similar evaluations by intensivists in two intensive care units (ICUs) in Strasbourg, France, between March 3 and April 3, 2020.

Six patients were excluded because of para-

of nasopharyngeal samples were
vere acute respiratory syndrome
(SARS-CoV-2). The median age
was 63 years, and the median Si
Physiology Score II at the time
examination was 52 (interquartil
65, on a scale ranging from 0
higher scores indicating greater
ness). Seven patients had had p
ding trans

Defining causality in COVID-19 and neurological disorders

Mark Ellul,[1,2,3] Aravinthan Varatharaj,[4,5] Timothy R Nicholson,[6] Thomas Arthur Pollak,[6] Naomi Thomas,[7,8] Ava Easton,[9] Michael S Zandi,[10] Hadi Manji,[10] Tom Solomon,[1,2,3] Alan Carson,[11] Martin R Turner,[12] Rachel Kneen,[1,3,13] Ian Galea,[4,5] Sarah Pett,[14,15] Rhys Huw Thomas,[7,16] Benedict Daniel Michael,[1,2,] CoroNerve Steering Committee

When faced with acute neurological presentations in a patient with COVID-19 how confident can one be that SARS-CoV2 is causal?

Journal of Alzheimer's Disease 76 (2020) 3–19
DOI 10.3233/JAD-200581
IOS Press

Review

Neurobiology of COVID-19

Majid Fotuhi[a,b,*], Ali Mian[c], Somayeh Meysami[d] and Cyrus A. F

BRAIN
A JOURNAL OF NEUROLOGY

The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings

Ross W Paterson, Rachel L Brown, Laura Benjamin, Ross Nortley, Sarah Wiethoff, Tehmina Bharucha, Dipa L Jayaseelan, Guru Kumar, Rhian E Raftopoulos, Laura Zambreanu

https://doi.org/10.1093/brain/awaa240
Published: 08 July 2020

ELSEVIER
ScienceDirect
Brain, Behavior, and Immunity
journal homepage: www.elsevier.com/locate/ybrbi
BRAIN, BEHAVIOR, and IMMUNITY

Encephalitis as a clinical manifestation of COVID-19

Dear Editor:

With great interest, we read the paper "Nervous system involvement after infection
speculated that

concluded. Treatment at this moment was largely supportive, including mannitol infusion. Intriguingly, the patient's consciousness generally ameliorated since Feb 20, and chest CT suggested a resolution of GGOs

Wits Journal of Clinical Medicine, 2020, 2(2) 135–140 http://dx.doi.org/10.18772/26180197.2020.v

Review Article

Neurological Involvement with COVID-19 Review

Andre Mochan[1] and Girish Modi[1]
[1]Division of Neurology, Department of Neurosciences, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study

Aravinthan Varatharaj, Naomi Thomas, Mark A Ellul, Nicholas W S Davies, Thomas A Pollak, Elizabeth L Tenorio, Mustafa Sultan, Ava Easton, Gerome Breen, Michael Zandi, Jonathan P Coles, Hadi Manji, Rustam Al-Shahi Salman, David K Menon, Timothy R Nicholson, Laura A Benjamin, Alan Carson, Craig Smith, Martin R Turner, Tom Solomon, Rachel Kneen, Sarah L Pett, Ian Galea, Rhys H Thomas*, Benedict D Michael*, on behalf of the CoroNerve Study Group†*

Summary

Background Concerns regarding potential neurological complications of COVID-19 are being increasingly reported, primarily in small series. Larger studies have been limited by both geography and specialty. Comprehensive characterisation of clinical syndromes is crucial to allow rational selection and evaluation of potential therapies. The
te the breadth of complications of COVID-19 across the UK that affected the brain.

Lancet Psychiatry 2020
Published Online
June 25, 2020
https://doi.org/10.1016/
S2215-0366(20)30287-X

JAMA Neurology | Review

Neuropathogenesis and Neurologic Manifestations of the Coronavir in the Age of Coronavirus Disease 2019

A Review

Adeel S. Zubair, MD; Lindsay S. McAlpine, MD; Tova Gardin, MD, MPP; Shelli Farhadian, MD, PhD; Deena E. Kuruvilla, MD; Serena Spudich, MD

REVIEW ARTICLE
Acta Neurologica Scandinavica
WILEY

Neurological Manifestations of COVID-19: A systematic review and current update

Abigail Whittaker[1] | Matthew Anson[1,2] | Amer Harky[3,4]

The Neurology of COVID-19

- Central Nervous System
  - Encephalopathies, Vasculitis, Stroke, Hypercoagulability, Meningoencephalitis, Myelitis
- Peripheral Nervous System
  - Guillain-Barré syndrome, Miller Fisher syndrome
- Muscle
  - Myopathy, Rhabdomyolysis

Neurology of COVID-19 due to SARS-CoV-2

Central Nervous System symptoms

Headache – 6%-8% (all patients), 13% (stroke patients)

Agitation & Delirium – 65-69% (58 ICU patients)

Impaired Consciousness – 15% severe cases, 22% fatal

Anosmia, hyposmia – 85% (cases from 12 hospitals)

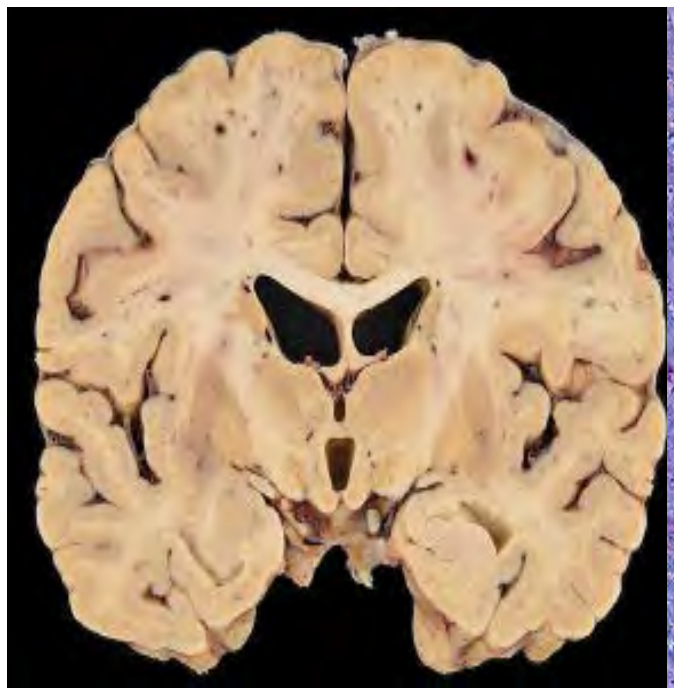
Dysgeusia – 88% (cases from 12 hospitals)

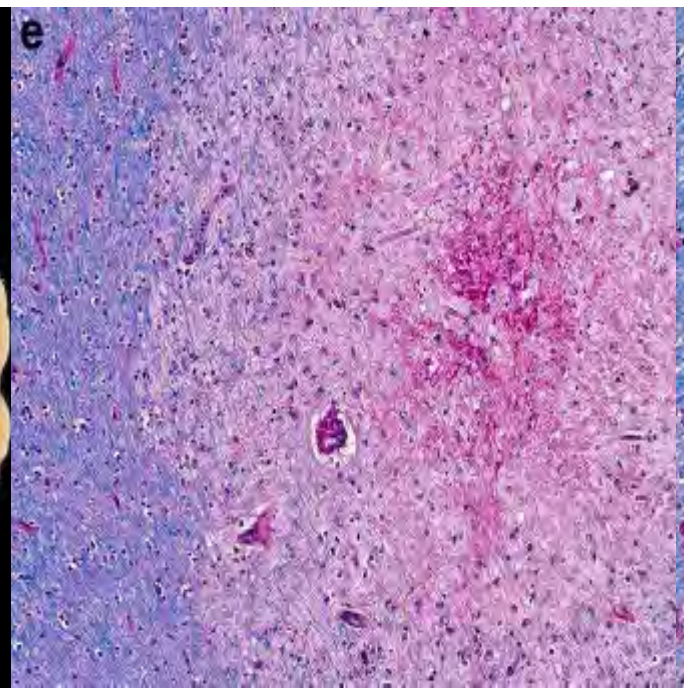
Acta Neuropathologica (2020) 140:1–6
https://doi.org/10.1007/s00401-020-02166-2

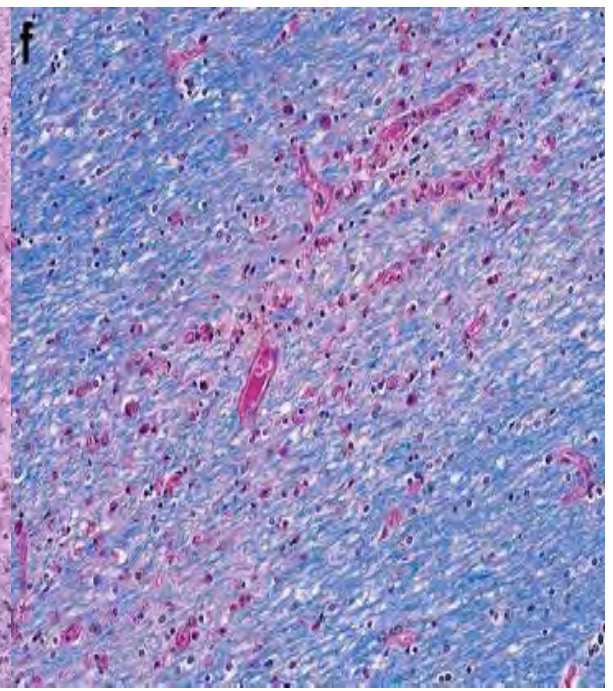
CASE REPORT

Neuropathology of COVID-19: a spectrum of vascular and acute disseminated encephalomyelitis (ADEM)-like pathology

R. Ross Reichard[1] · Kianoush B. Kashani[2] · Nicholas A. Boire[1] · Eleni Constantopoulos[1] · Yong Guo[3] · Claudia F. Lucchinetti[3]



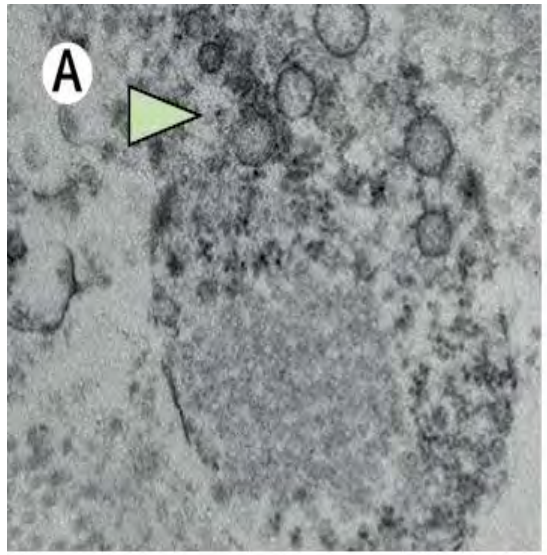


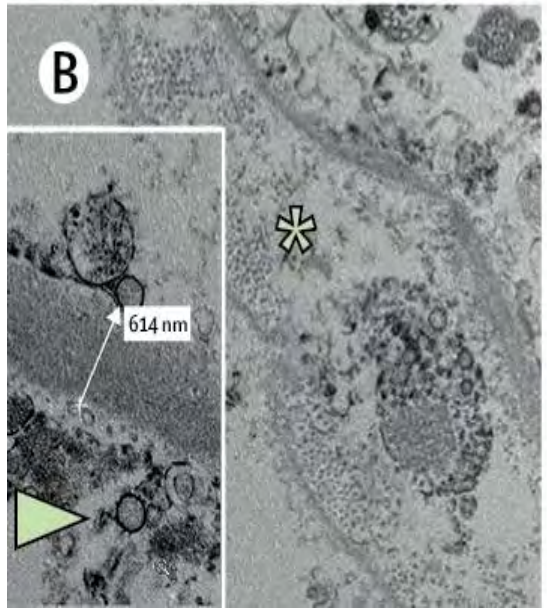


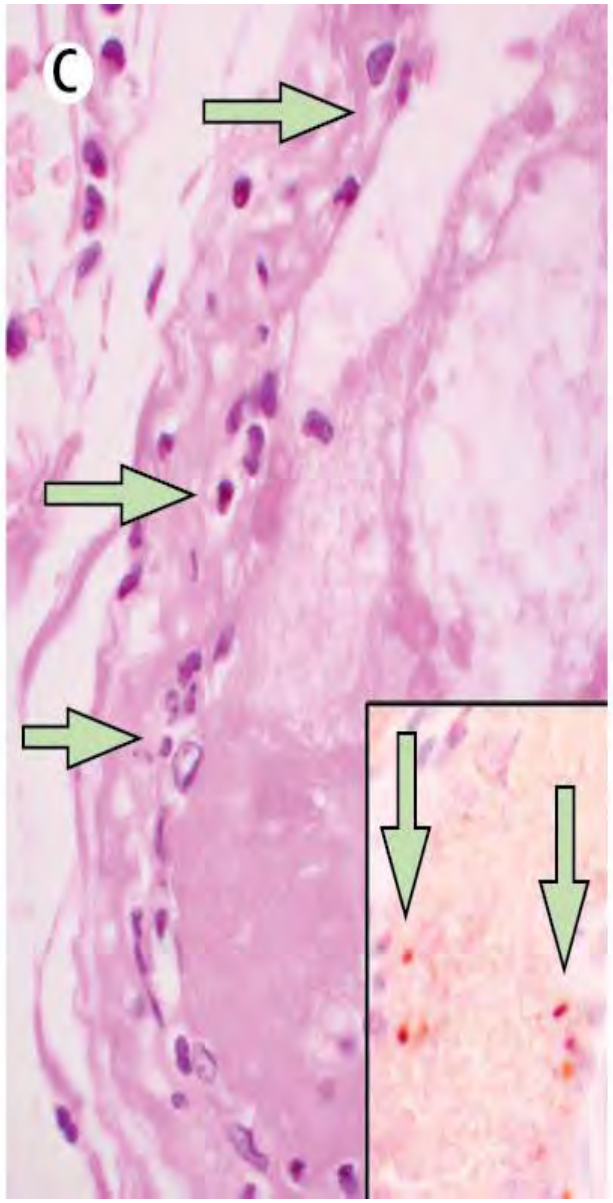
How Does COVID-19 Affect The Nervous System

- Endothelial cells – ACE2 receptors to enter cells and membrane TMPRSS2 serine protease cleave the viral spike protein and facilitate cell entry – blood vessels
- Hypercoagulability, thromboembolic complications
- Virus is Neurotropic – Invasion of the CNS – Olfactory system via ACE2 receptor attachment and membrane TMPRSS2
- Hyper-inflammation – activated macrophages – “cytokine storm”
- Altered immune system – Post-infectious autoimmune disorders

www.thelancet.com Published online April 17, 2020

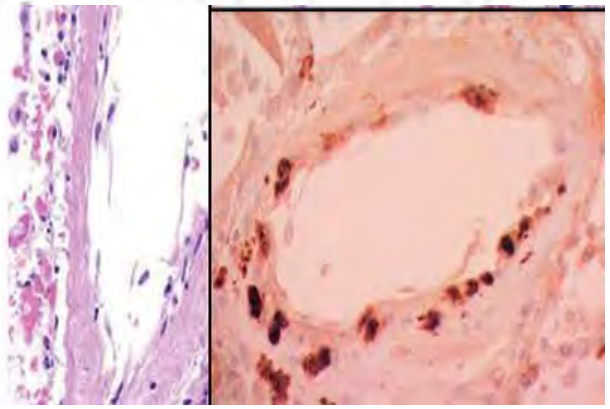






Endothelial cell infection and endotheliitis in COVID-19

Zsuzsanna Varga, Andreas J Flammer, Peter Steiger, Martina Haberecker, Rea Andermatt, Annelies S Zinkernagel, Mandeep R Mehra, Reto A Schuepbach, *Frank Ruschitzka, Holger Moch



blood
Perspective

COVID-19 and its implications for thrombosis and anticoagulation

Jean M. Connors[1] and Jerrold H. Levy[2-4]

Summary of findings

- **Coagulopathy is manifest as elevated fibrinogen, elevated D-dimers, and minimal change in PT, aPTT, and platelet count in early stages of infection**
- **Increasing IL-6 levels are correlated with increasing fibrinogen levels – activated macrophages**

The NEW ENGLAND JOURNAL of MEDICINE

Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young

We report five cases of large-vessel stroke in patients younger than 50 years of age who presented to our health system in New York City. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was diagnosed in all five patients.

Cough, headache, and chills lasting 1 week developed in a previously healthy 33-year-old woman (Patient 1) (Table 1). She then had progressive dysarthria with both numbness and weakness in the left arm and left leg over a period of 28 hours. She delayed seeking emergency care because of fear of Covid-19. When she presented to the hospital, the score on the National

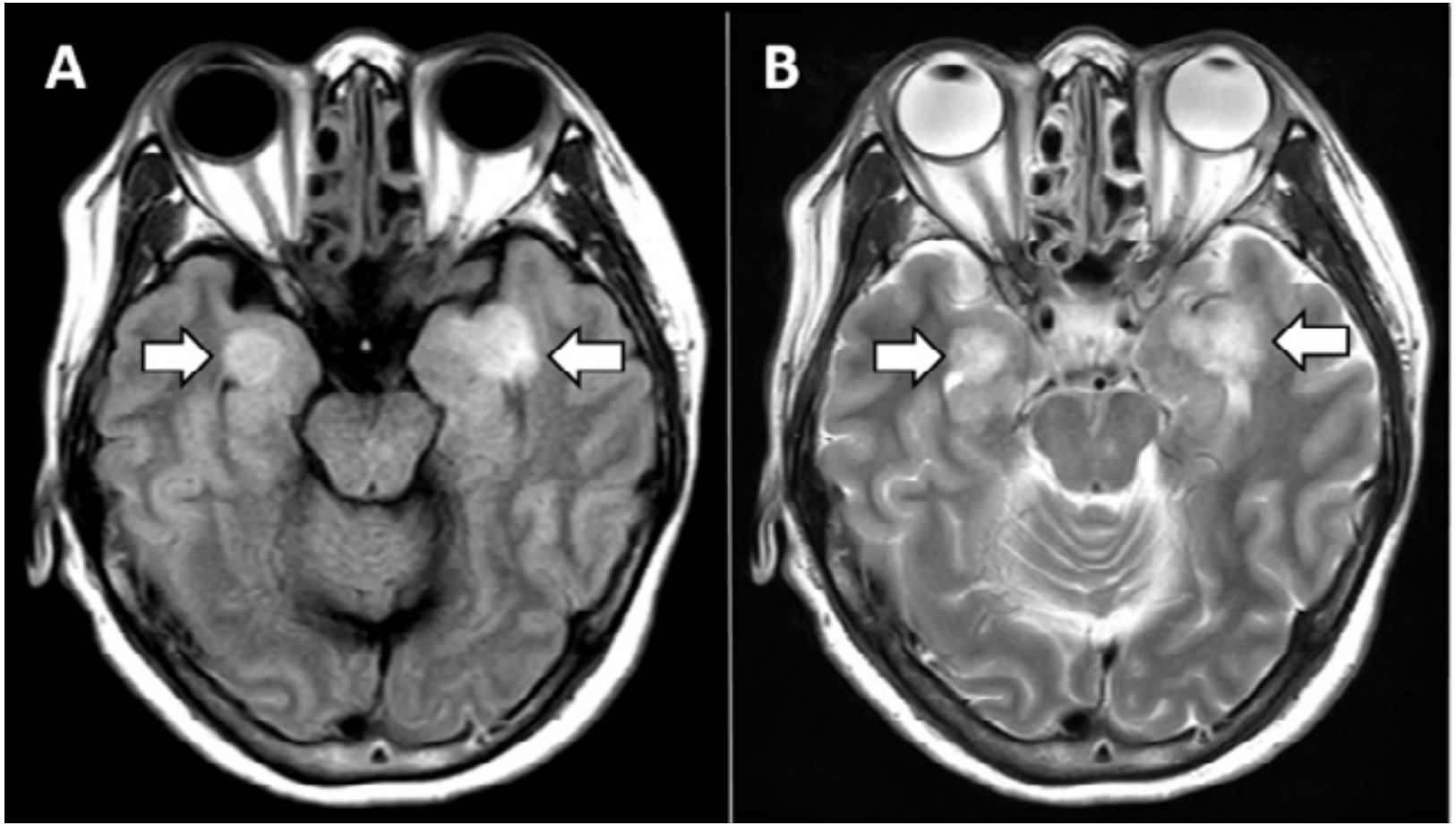
2020, a total of five patients (including the aforementioned patient) who were younger than 50 years of age presented with new-onset symptoms of large-vessel ischemic stroke. All five patients tested positive for Covid-19. By comparison, every 2 weeks over the previous 12 months, our service has treated, on average, 0.73 patients younger than 50 years of age with large-vessel stroke.

On admission of the five patients, the mean NIHSS score was 17, consistent with severe large-vessel stroke. One patient had a history of stroke. (

Published online 4/28/2020

COVID-19–associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI Features

Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. ***Radiology 2020***



Cerebrovascular Disease in Patients with COVID-19: A Review of the Literature and Case Series.

S.Reddy,T. Gang,.. J. Volpi, V. Misra, D. Chiu, R. Gadhia, S. Savitz – Case Rep Neurol-2020;12:199.

...

- Case series of 12 patients, 10 patients had an ischemic stroke, two had intracerebral hemorrhage.
- Etiology was determined to be embolic without a clear cause identified in 6 ischemic stroke patients, while the remaining had an identifiable source of stroke.
- The majority of the patients had elevated inflammatory markers such as D-dimer and interleukin-6.
- In patients with embolic stroke of unclear etiology, COVID-19 may have played a direct or indirect role in the processes that eventually led to the strokes while in the remaining cases, it is unclear if infection contributed partially or was an incidental finding.

Coronaviruses are Neurotropic

- **Most avian, feline, canine, porcine, bovine and equine coronaviruses cause respiratory and enteric diseases**
- **Porcine hemagglutinating encephalomyelitis virus causes respiratory disease & encephalomyelitis in pigs**
- **Neurotropic mouse hepatitis virus causes CNS demyelination**
- **HCoV-OC43 found in ADEM and encephalitis**
- **HCoV-229E and HCoV-OC43 found in 44% of MS brains**

ScienceAdvances

RESEARCH ARTICLES

Cite as: D. H. Brann *et al.*, *Sci. Adv* 10.1126/sciadv.abc5801 (2020).

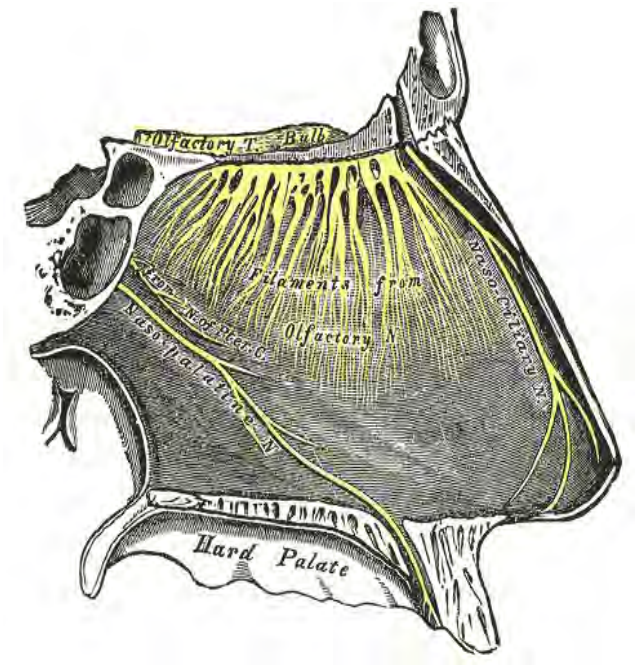
Non-neuronal expression of SARS-CoV-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19-associated anosmia

Bulk sequencing demonstrated that mouse, non-human primate and human olfactory mucosa expresses two key genes involved in CoV-2 entry, ACE2 and TMPRSS2. However, single cell sequencing revealed that ACE2 is expressed in support cells, stem cells, and perivascular cells, rather than in neurons. Immunostaining confirmed these results and revealed pervasive expression of ACE2 protein in dorsally-located olfactory epithelial sustentacular cells and olfactory bulb pericytes in the mouse. These findings suggest that CoV-2 infection of non-neuronal cell types leads to anosmia and related disturbances in odor perception in COVID-19 patients.

SARS-CoV-2 Neurotropism

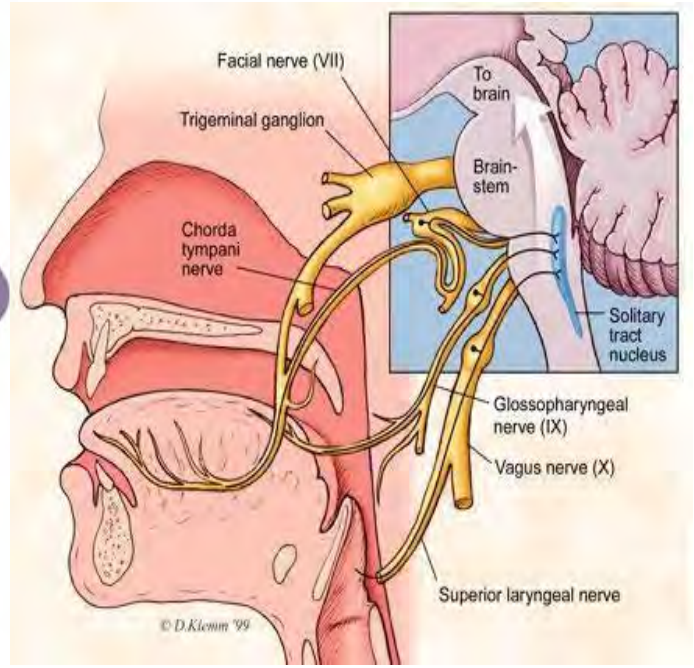
- **CN I Olfactory: Nasal mucosa ACE2 receptors & TMPRSS2, nasal filaments, olfactory bulbs, olfactory tracts to rhinencephalon: ICU delirium and psychomotor agitation** (Helms et al. *N Engl J Med* 4 June 2020)
- **CN V Trigeminal: Rhinopharyngeal-buccal mucosa, cornea, conjunctiva, Gasserian ganglion to brainstem trigeminal nucleus**
- **CN VII Facial nerve: Taste anterior 2/3 tongue, chorda tympani to pontine geniculate nucleus**
- **CN IX Glossopharyngeal: Taste posterior 1/3 tongue, oropharynx, carotid sinus to nucleus tractus solitarii** (Porzionato et al. *Lung Cell Mol Physiol* 5 Aug 2020)
- **Oropharyngeal dysphagia** (Aoyagi et al. *Dysphagia* 12 June 2020)
- **CN X Vagus: Mechanoreceptors and chemoreceptors in lung and respiratory tract to dorsal motor nucleus vagus and nucleus ambiguus** (Li et al. *J Med Virol* 24 Feb 2020)

Viral Highways to the Brain
(Cranial Nerves I, V, VII, IX, X)



Olfactory Nerve (CN I)
Olfactory Tract & Bulb
Olfactory Filaments

Trigeminal Nerve (CN V)
Trigeminal Ganglion
Ophthalmic Nerve (v 1)
Maxillary Nerve (v 2)
Mandibular Nerve (v 3)



Facial Nerve (CN VII)
Glossopharyngeal Nerve(CN IX)
Vagus Nerve (CN X)

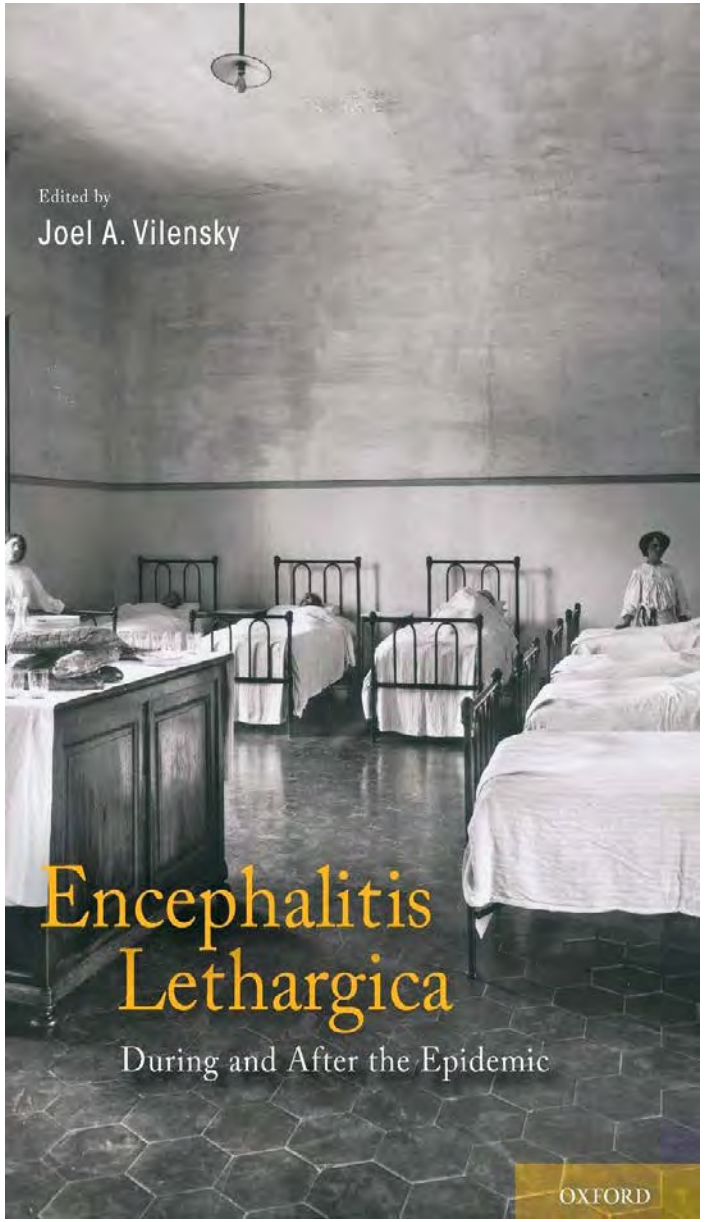
Olfactory transmucosal SARS-CoV-2 invasion as port of Central Nervous System entry in COVID-19 patients

bioRxiv- Meinhardt et al, 9-2020

- Viral RNA present in the brain and cerebrospinal fluid, ? portal of viral entry.
- Brains of 32 patients dying from COVID-19 – CNS infarction in oro- and pharyngeal regions due to cerebral thromboembolism present, but also **evidence of SARS-CoV-2 neurotropism.**
- **SARS-CoV-2 can enter the CNS – via the neuro-mucosal interface in the olfactory mucosa. Then SARS-CoV-2 follows defined neuroanatomical structures, including the primary respiratory and cardiovascular control center in the medulla oblongata.**

Neurotropic Viruses and Sleep

- H1N1 influenza virus of avian origin (Spanish flu pandemic) 1915-18
- H2N2 influenza type A (Asian flu) Kleine-Levin syndrome 1957-58
- Influenza B (Japan) Kleine-Levin syndrome 1957-58
- H1N1 influenza epidemic (China) Narcoleptic syndromes 2009-2010
- Murine H1N1 intranasal infection produced narcolepsy-like syndromes
  - Virus infected the olfactory nerves (CN I)
  - Olfactory bulb glomerular layer (day 14)
  - Mitral and granular cells (day 28)
  - Retrograde invasion of orexin- and melanin-concentrating-hormone nuclei
  - Lateral hypothalamus (day 28)
  - Pontine dorsal raphe and locus coeruleus nuclei



OXFORD MEDICAL PUBLICATIONS

ENCEPHALITIS LETHARGICA ITS SEQUELAE AND TREATMENT

BY

CONSTANTIN VON ECONOMO

PROFESSOR OF INTERNAL AND NEUROLOGY IN THE UNIVERSITY OF VIENNA

TRANSLATED AND ADAPTED BY

K. O. NEWMAN, M.D.

PATHOLOGIST TO THE [illegible] INSTITUTE AND CITY MENTAL HOSPITAL OXFORD

With 21 Illustrations

OXFORD UNIVERSITY PRESS
LONDON : HUMPHREY MILFORD
1931

Leslie A Hoffman, Joel A Vilensky

Encephalitis lethargica: 100 years after the epidemic

Brain, 140: 2246–2251, 2017

- **Encephalitis lethargica is a neurological syndrome of postencephalitic parkinsonism – with stiffness and bradykinesia as well as psychiatric manifestions.**
- **Beginning in the winter of 1916–17, and continuing into the 1930s. The exact number afflicted – estimated to be more than one million worldwide.**
- ?? An autoimmune disorder caused by antibodies against NMDA receptors. Anti-NMDA receptor encephalitis.

STARTING OUR CENTER FOR TRANSLATIONAL NEURAL PROSTHETICS & INTERFACES

Gavin W. Britz MD, MPH, MBA, FAANS, FACS
Professor and Chairman, Department of Neurosurgery
Houston Methodist
Professor, Weill Cornell, NY
Houston, Texas

HOUSTON Methodist LEADING MEDICINE

The Brain Implants That Could Change ... - The New York Times
https://www.nytimes.com/2020/08/28/opinion/sunday/brain-machine-artificial...

DEPT. OF NEUROSURGERY
MAJOR RESEARCH CENTERS

HOUSTON Methodist LEADING MEDICINE

Kenneth R. Peak Brain & Pituitary Treatment Center

Kenneth R. Peak Center for Brain and Pituitary Tumor Treatment and Research provides world-class personalized neurosurgical and oncological treatments for patients with brain, spine and pituitary tumors in a compassionate environment geared toward scientific advances, education and research.

KENNETH R. PEAK BRAIN & PITUITARY TREATMENT CENTER

David Baskin, MD, FAANS, FACS
Peak Center Director
Kenneth R. Peak Presidential Distinguished Chair
Director of Brain Metastasis, Glial Tumor, and Pituitary Tumor and Disorder Initiative
Co-Director, Skull Base Tumor Initiative
View CV

CENTER FOR NEUROREGENERATION

Our mission is to generate therapies for people who suffer from chronic paralysis and neurologic loss due to devastating injury, stroke or degenerative disease. The Center for Neuroregeneration

CENTER DIRECTOR

Philip J. Horner, PhD
Scientific Director, Neuroregeneration
Co-Director, Regenerative & Restorative Neurosurgery
Vice Chairman-Research,Neurosurgery
Houston Methodist Research Institute

CENTER FOR NEUROPROSTHETICS

Gavin W. Britz, MBBCh, MPH, MBA, FAANS
Chair, Department of Neurosurgery

ENGINEERING IS THE BEGINNING AND THE END IN THE MODERN WORLD

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Climate change

Sustainable energy

Improved food sources

***ENGINEERING** IS GOING TO SOLVE THE WORLD'S PROBLEMS*

Eco friendly waste control, including plastics

Eco friendly travel, including space

Improved military protection

WHAT IS NEUROPROSTHETICS

HOUSTON Methodist LEADING MEDICINE

UTILIZATION OF ENGINEERING TO SOLVE BIOMEDICAL PROBLEMS IN THE BRAIN AND SPINAL CORD

DARPA

HOUSTON Methodist LEADING MEDICINE


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Neurorestoration
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Repair – Replace – Optimize
Neurosurgery/Neurology/Psychiatry/Neurorehabilitation
Neural Engineering/Computational Neuroscience/Regenerative Medicine

NEURAL ENGINEERING

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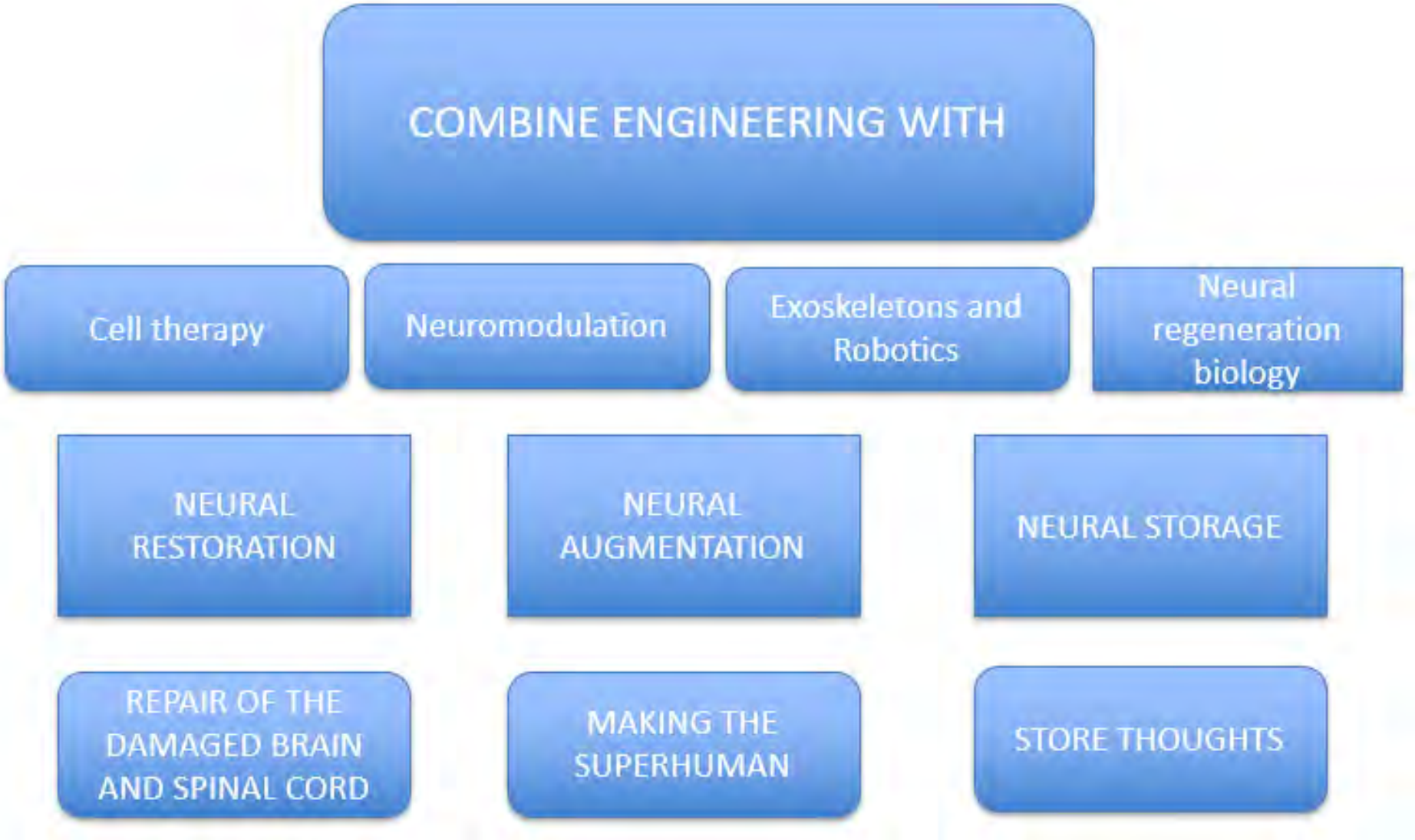

EVOLUTION OF TECHNOLOGY

HOUSTON Methodist LEADING MEDICINE

CELL PHONE WAS DEVELOPED FOR EASE OF COMMUNICATION
EVOLVED TO WALKING AROUND WITH A HIGH-POWERED COMPUTER

NEXT PHASE, COMPUTER INCORPORATED INTO OUR BRAINS

NATURAL QUESTION

HOUSTON Methodist LEADING MEDICINE

ARE HUMAN BRAIN CHIPS JUST FUTURISTIC ?

NO, A FEW PATIENTS HAVE THEM CURRENTLY IMPLANTED

NEURAL ENGINEERING SOLVING PARALYSIS

HOUSTON Methodist LEADING MEDICINE

- 2 implants, with 64 electrodes on each implant, were surgically placed on the surface of the brain, covering the parts of the brain that control movement
- The electrodes on each implant read the patient's brain activity and transferred the instructions to a computer
- Brainwaves were read by computer software and turned into instructions for controlling the exoskeleton
- When patient thinks "walk," there is a set of command movements in the robotic suit that move the patient's legs forward

Array recording from a "Utah" array implanted in human posterior parietal cortex

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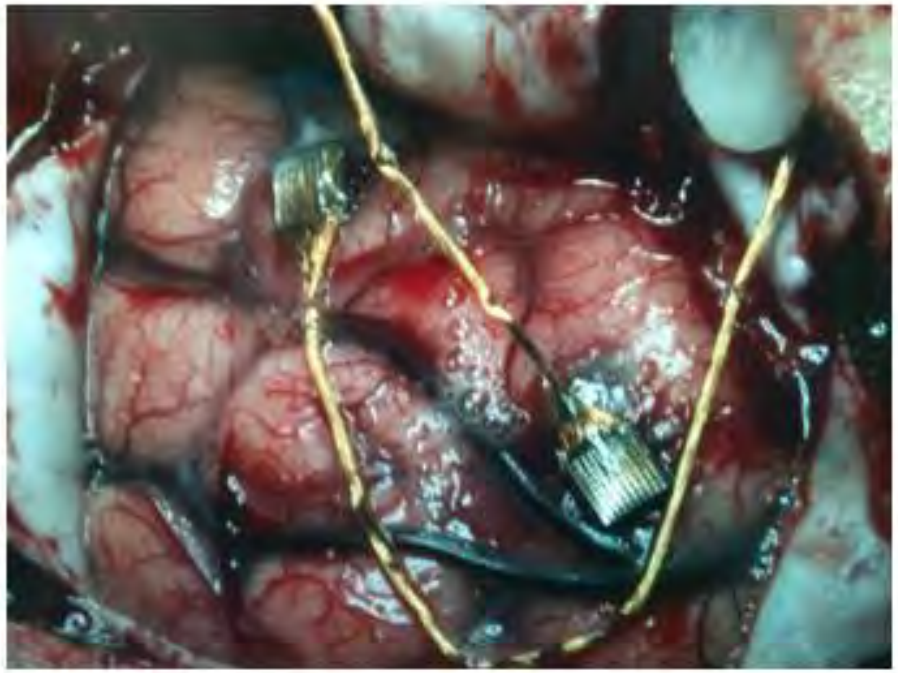
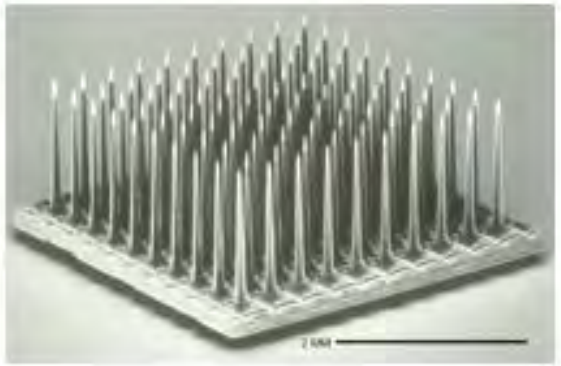
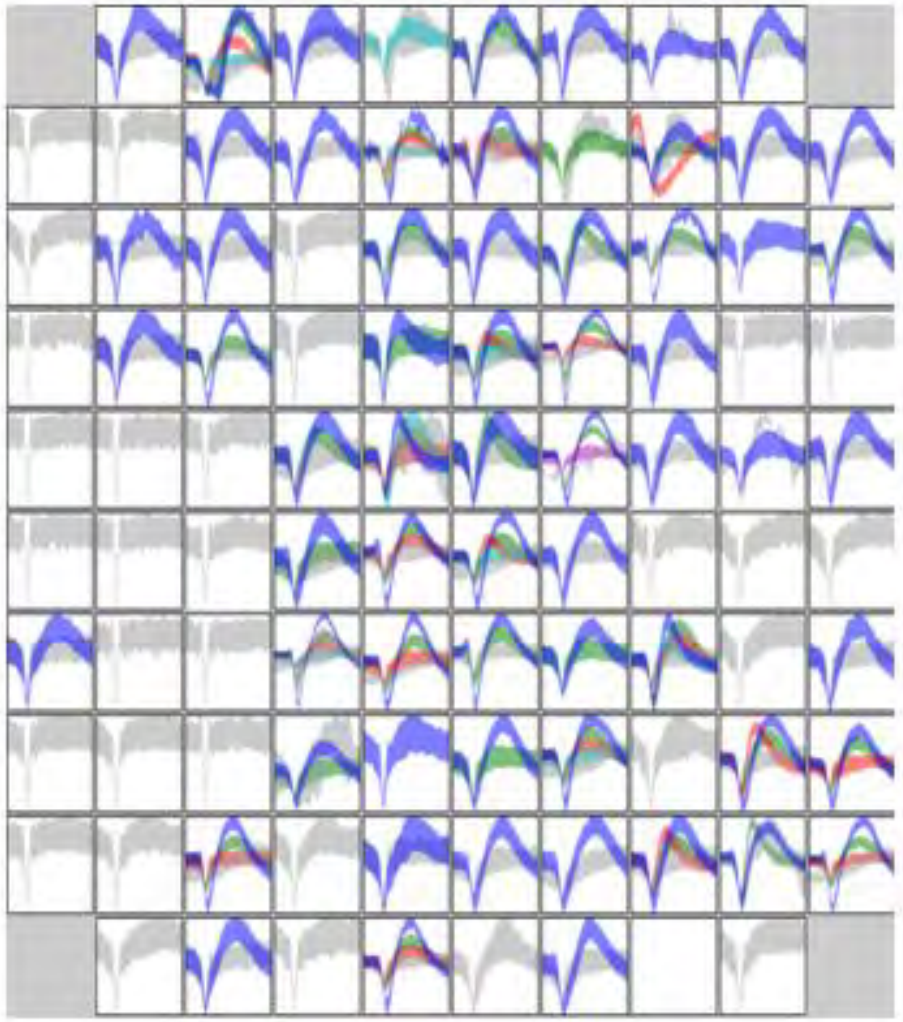
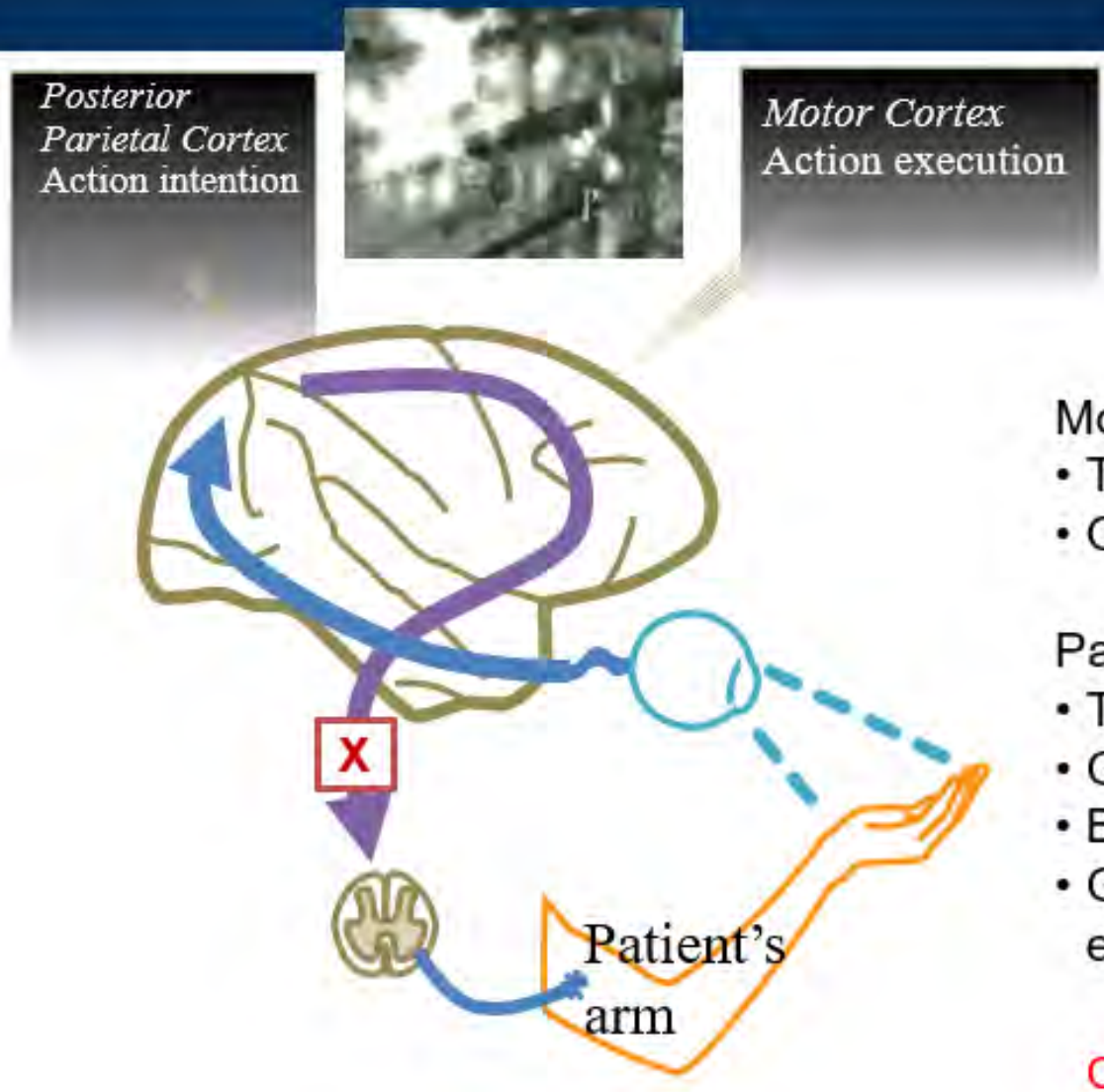






Intent signals for cortical neural prosthetics



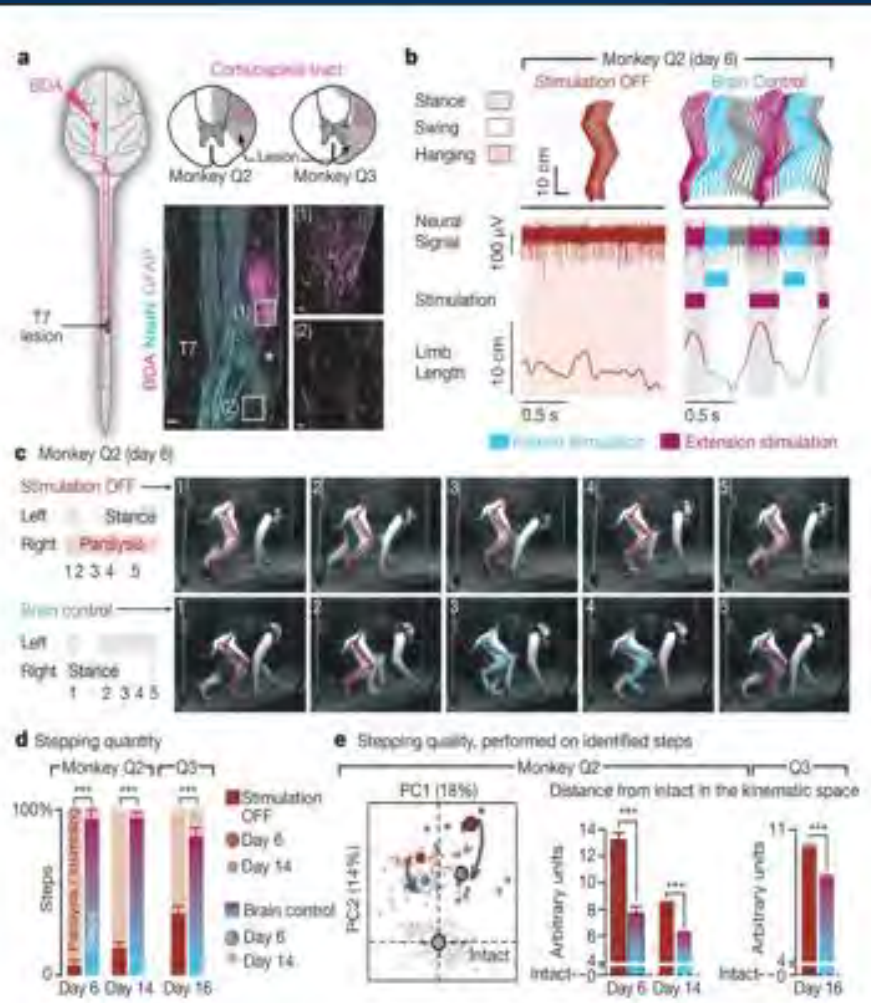
Motor Cortex:
- Trajectory
- One limb

Parietal Cortex:
- Trajectory
- Goal (fast ~ 200 ms)
- Both limbs
- Grasp (single cells convey entire grasp)

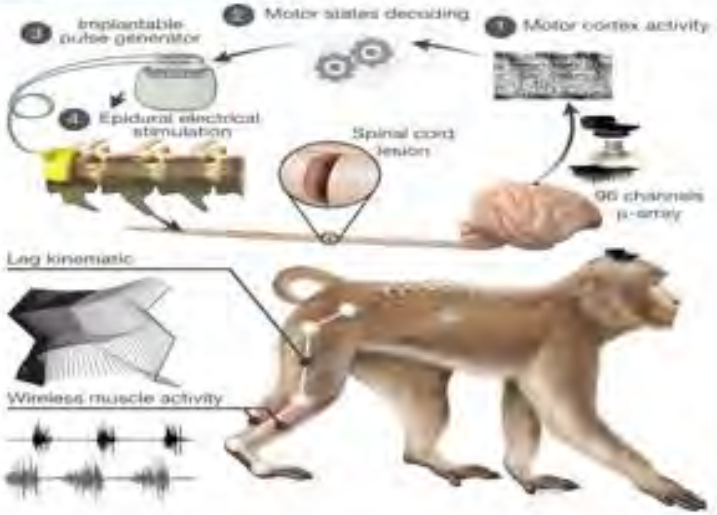
Courtesy of Richard Andersen

THE BRAIN–SPINE INTERFACE ALLEVIATES GAIT DEFICITS AFTER SPINAL CORD INJURY

HOUSTON Methodist LEADING MEDICINE



M Capogrosso *et al. Nature* **539**, 284–288 (2016)
doi:10.1038/nature20118



A BRAIN SPINAL INTERFACE ALLEVIATING LOCOMOTOR DEFICITS AFTER SPINAL CORD INJURY

Supplementary Video 1

Funding

Partners

nature

MEMORY

HOUSTON Methodist LEADING MEDICINE

Goal: Develop a Biomimetic Model of Hippocampus to Serve as a Neural Prosthesis for Lost Cognitive/Memory Function

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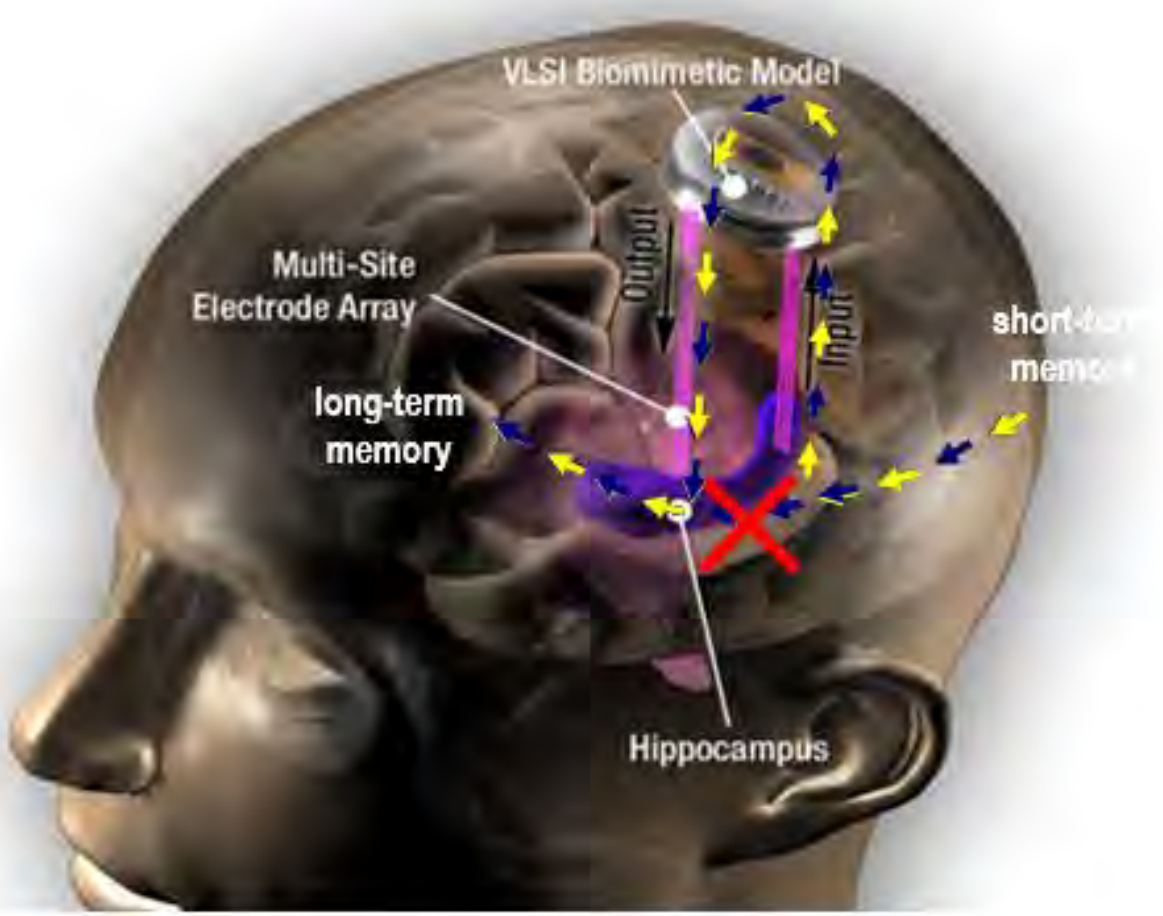
Strategy:

1. Biomimetic model/device that mimics signal processing function of hippocampal neurons/circuits
2. Implement model in VLSI for parallelism, rapid computational speed, and miniaturization
3. Multi-site electrode recording/stimulation arrays to interface biomimetic device with brain
4. Goal: to "bypass" damaged brain region with biomimetic cognitive function



Courtesy of Ted Berger

Neuropace RNS

HOUSTON Methodist LEADING MEDICINE

ORIGINAL ARTICLE

A Single-Center Experience with the NeuroPace RNS System: A Review of Techniques and Potential Problems

Brian Lee[1], Muhammad N. Zubair[1], Yvette D. Marquez[1], David M. Lee[1], Laura A. Kalayjian[2], Christianne N. Heck[2], Charles Y. Liu[1,2]

INTRODUCTION: The clinical results for the RNS System (NeuroPace, Mountain View, California, USA) closed-loop responsive neurostimulator for the treatment of medically intractable partial-onset seizures have been encouraging. The University of Southern California (USC) Neurorestoration Center and the Keck Hospital of USC have become the world's first institutions to implant an RNS System post U.S. Food and Drug Administration (FDA) approval. As one of the study centers, we review our experience with our group of patients who have been implanted with the RNS System.

METHODS: A total of 40 surgeries by a single surgeon were performed on 10 patients (7 male and 3 female) with an average age of 39.2 years (24–66 years) and were followed for an average of 45 months (30–54 months). The average age at seizure onset was 14 years (birth–37 years) with an average of 4.7 (3–12) failed antiepileptic drugs. We reviewed the patients' charts for complications from the surgeries including infections requiring surgical intervention, hematomas, hardware failures, and death.

RESULTS: Of the 40 surgeries, there were 10 initial implantations of the neurostimulator and leads, 24 neurostimulator replacements for expected end of neurostimulator service, 2 incision and drainage procedures (I & Ds) for soft tissue infection followed by 1 explantation and 1 reimplantation (same patient), and 2 revisions because of one lead that was damaged at the exit point between the skull and a titanium mesh and the second lead that was damaged at an acute bend over the skull (same patient). Eight of the patients had no complications and underwent an average of 2.7 neurostimulator replacements over 7 consecutive years to date. Each patient underwent routine postoperative computed tomography imaging of the brain, and none had any intracranial hematomas or misplaced leads requiring revision surgery. Finally, there were no deaths in our patient population.

CONCLUSIONS: Our experience with the NeuroPace RNS System over an average follow-up of 45 months suggests that the surgery and device are safe when placed by an experienced surgeon. Although there were no clinically significant hematomas or patient deaths, we did have 1 patient each with infection and lead damage at the point of exit from the skull. We compare the results of this study with other neuromodulation procedures for epilepsy to evaluate the safety and complications associated with the RNS System. Our initial experience suggests that the RNS System can be readily incorporated into an active epilepsy surgical center.

INTRODUCTION

For patients who suffer from medically refractory epilepsy, surgery is often explored as an option if they have a resectable lesion that can be identified as the focus of

Key words
- Epilepsy
- Neuromodulation
- NeuroPace
- RNS System
- Safety

Abbreviations and Acronyms
AED: Antiepileptic drug
BMI: Brain-machine interface
DBS: Deep brain stimulation
ECoG: Electrocorticogram
EEG: Electroencephalogram
FDA: U.S. Food and Drug Administration
I & D: Incision and drainage
RNS: Responsive neurostimulator
SANTE: Stimulation of the anterior nucleus of the thalamus for epilepsy
SOZ: Seizure onset zone
USC: University of Southern California
VNS: Vagus nerve stimulation

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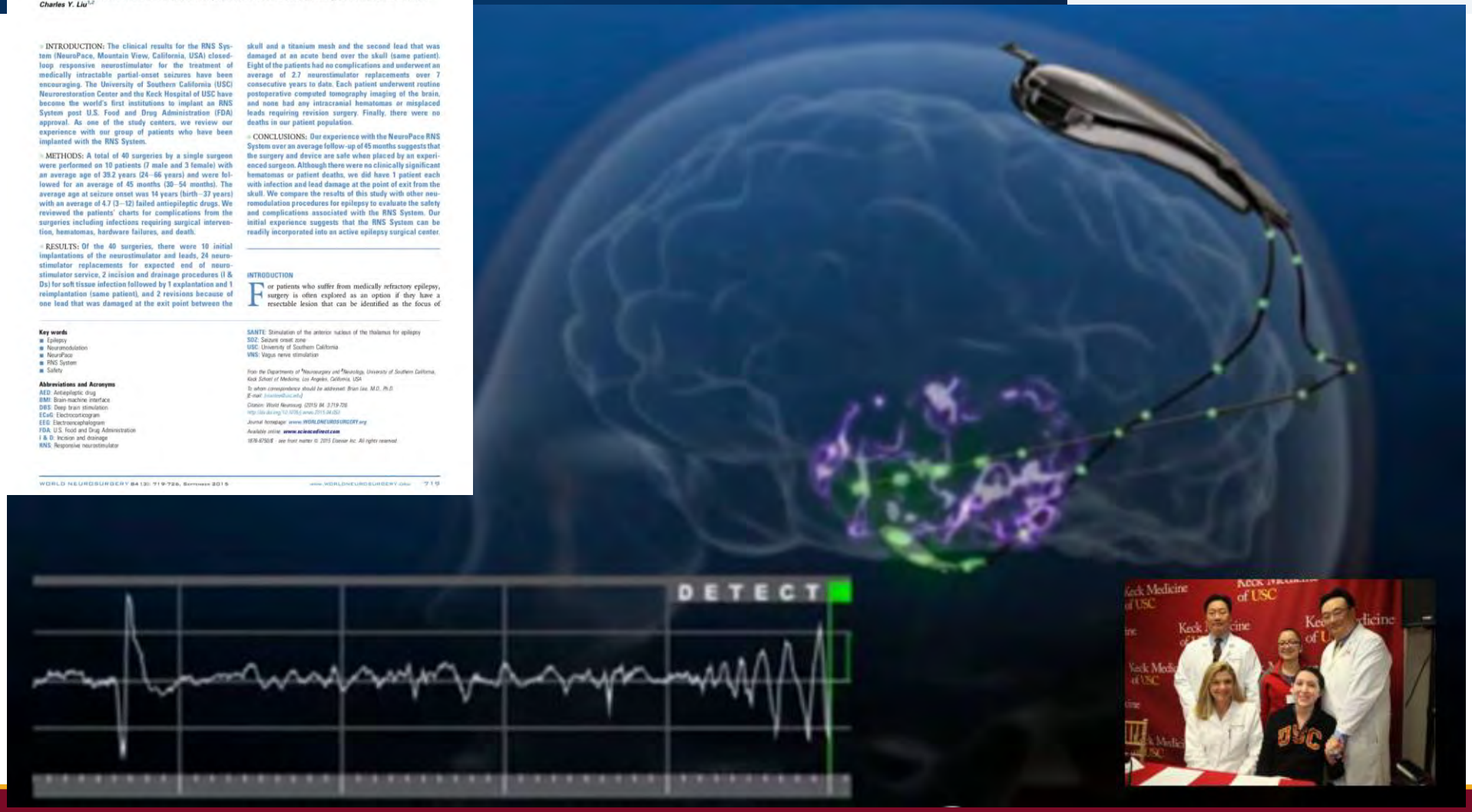
http://dx.doi.org/10.1016/j.wneu.2015.04.043
Journal homepage: www.WORLDNEUROSURGERY.org
Available online: www.sciencedirect.com



Keck School of Medicine of USC

ISRAELI GROUP

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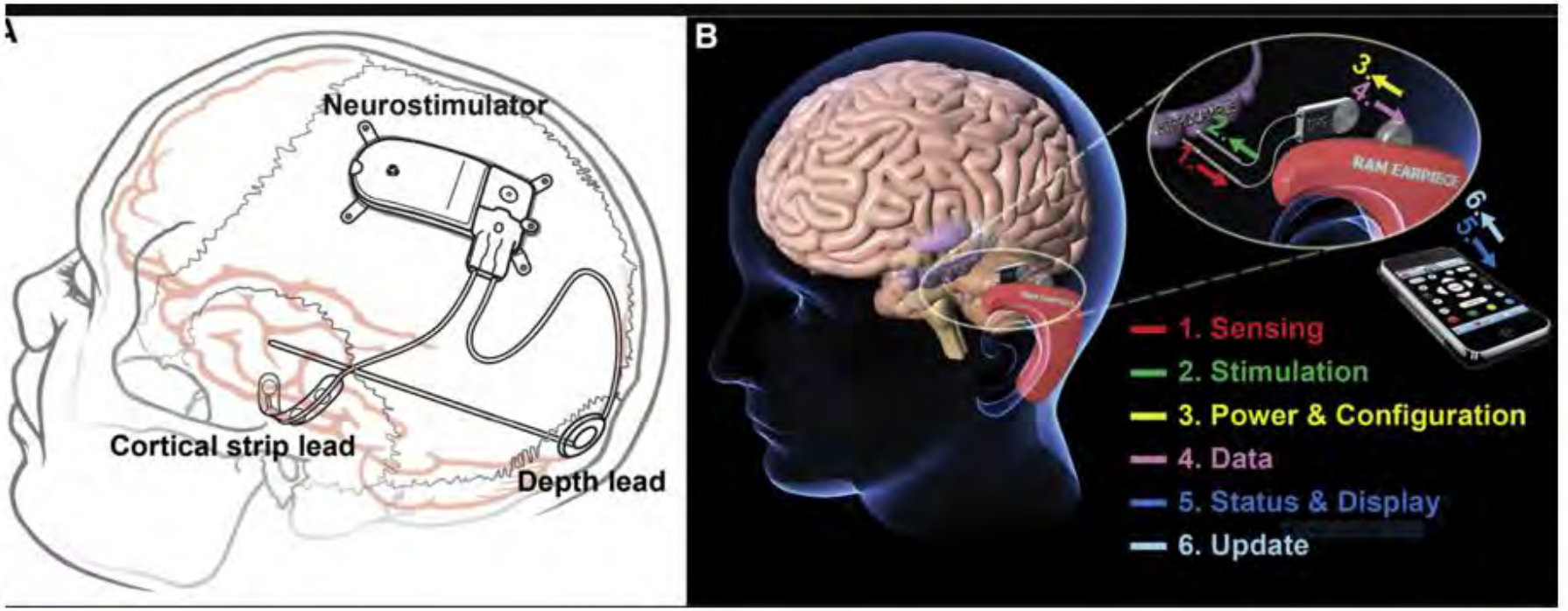

Press

Neuron
Perspective

Modulation of Human Memory by Deep Brain Stimulation of the Entorhinal-Hippocampal Circuitry

Emily A. Mankin[1] and Itzhak Fried[1,2,3,*]
[1]Department of Neurosurgery, University of California, Los Angeles, Los Angeles, CA 90095, USA
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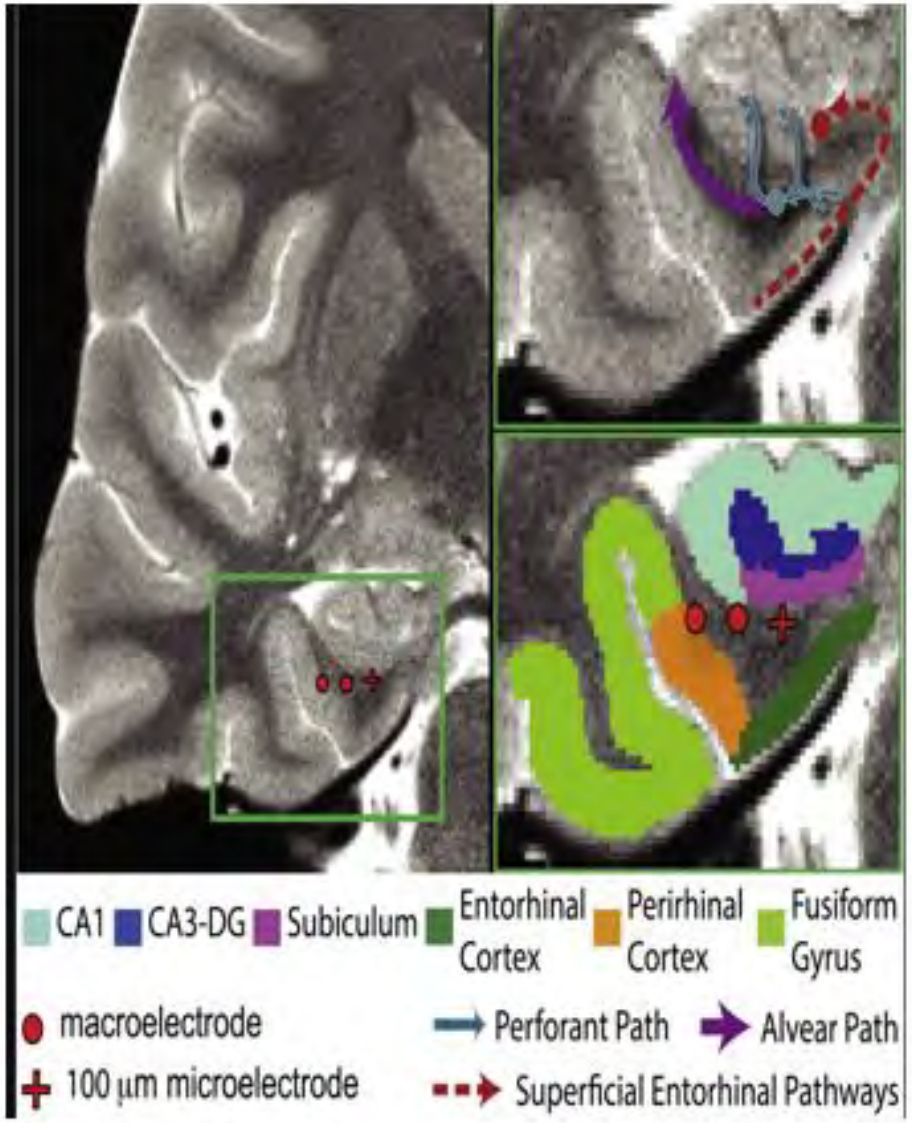
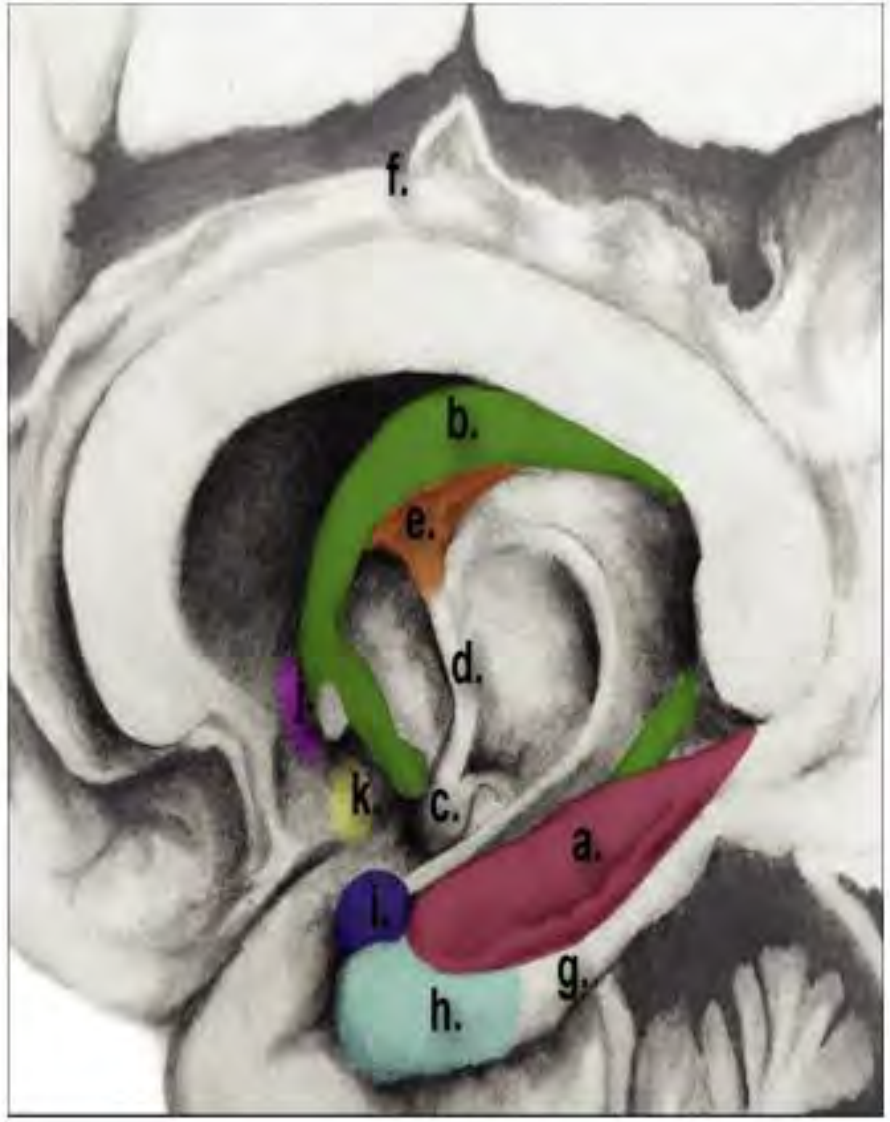
https://doi.org/10.1016/j.neuron.2020.02.024


CA1
CA3-DG
Subiculum
Entorhinal Cortex
Perirhinal Cortex
Fusiform Gyrus
macroelectrode
100 µm microelectrode
Perforant Path
Alvear Path
Superficial Entorhinal Pathways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OUR CENTER FOR TRANSLATIONAL NEURAL PROSTHETICS & INTERFACES

HOUSTON Methodist LEADING MEDICINE

Core Faculty

- PHYSICAL SPACE
  - A Living Human Laboratory at HM
  - Operating Rooms at HM
  - BRC Campus (Rice)
  - Primate Center at HM
  - Large Animal lab at HM
- CORE PERSONNEL
  - 7 Engineers from Rice Current Faculty
  - 3 additional Engineers jointly hired by HM and Rice
  - 7 Neurosurgeons from HM
  - Awesome PM&R Physicians
  - Center Neuroregeneration Faculty

Collaborators

- Charles Liu – Neurosurgeon at USC
- CALTECH Engineers
- Texas A&M Engineers

FOCUS AREAS AS WE HIRE SCIENTISTS

- SPINAL CORD INJURY INCLUDING HAND FUNCTION
- MEMORY/ EPILEPSY
- CORTICAL MOTOR/ SENSATION

STARTING AT METHODIST IN JANUARY: FUNCTIONAL/PERIPHERAL NERVE SURGEON

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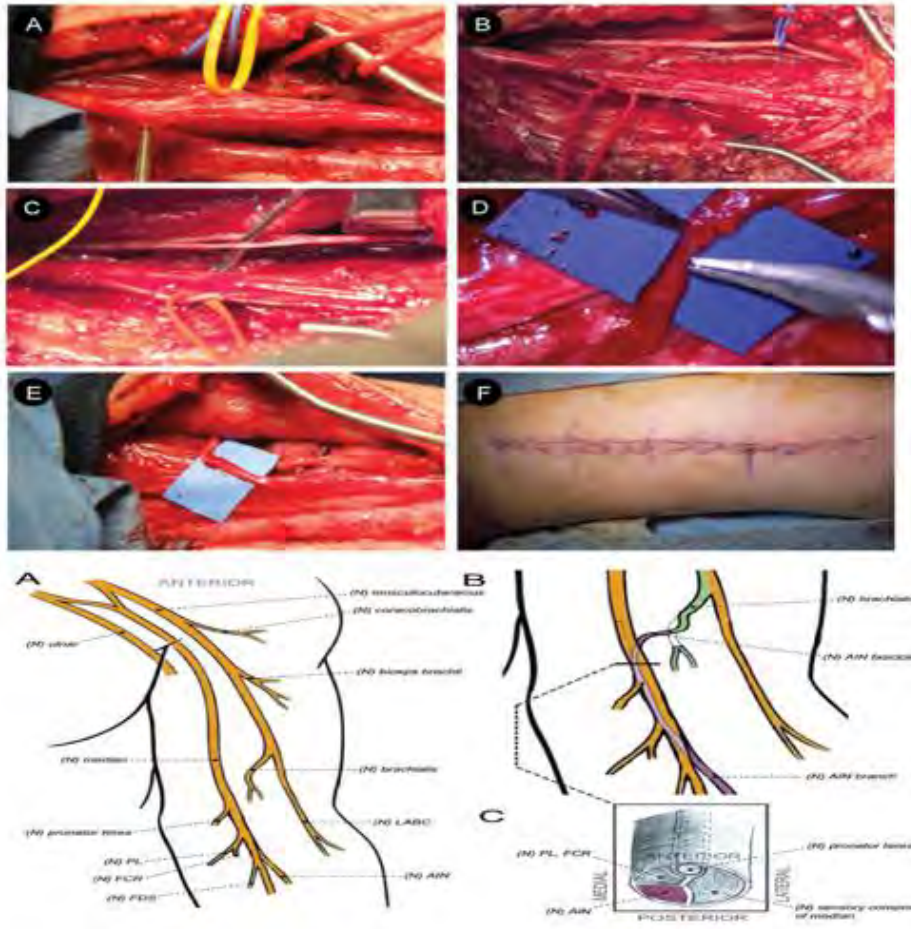
AMIR H. FARAJI, MD, PhD

Novel Peripheral Nerve Transfers to Improve Function



Patient with a C7 ASIA A Low Cervical Spinal Cord Injury

Brachialis Nerve to Anterior Interosseous Nerve for Finger and Thumb Flexion

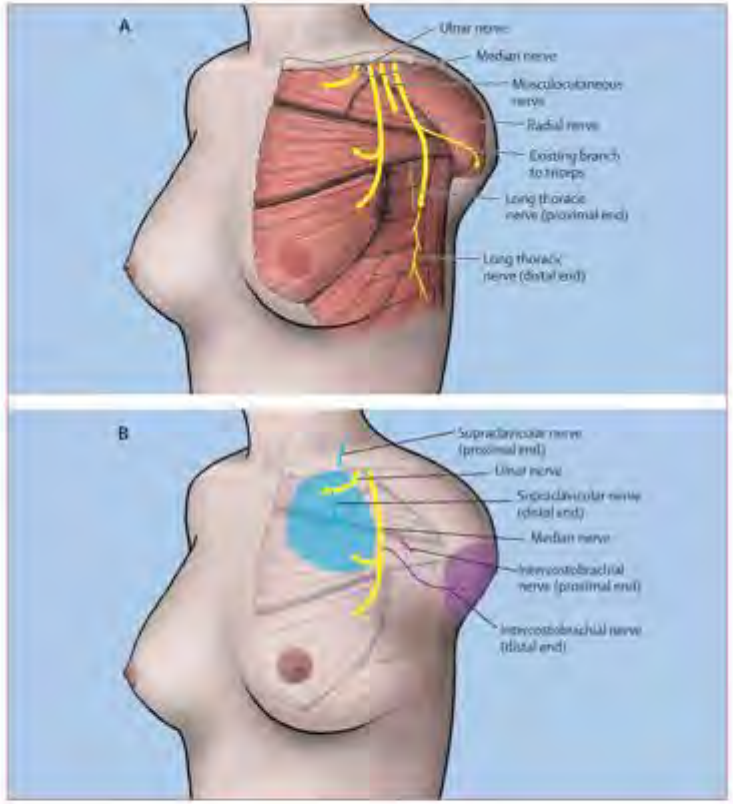
TARGETED REINNERVATION FOR NEURAL PROSTHETIC CONTROL

HOUSTON Methodist LEADING MEDICINE

Pre-Operative Amputation with Proximal Nerve Stumps Identified

Musculocutaneous, Median, Radial, and Ulnar Nerves were identified in the amputation stump and trimmed back to intact fascicles.

The musculocutaneous, median, and ulnar nerves were routed to distinct parts of pectoralis major muscle. The long thoracic nerve was coapted to the radial nerve. The supraclavicular cutaneous nerve coapted to ulnar nerve. The intercostobrachial cutaneous nerve coapted to the median nerve.



Kuiken, T. A., et. al. J. Lancet. 2007, 369, 371-380.

TARGETED REINNERVATION FOR NEURAL PROSTHETIC CONTROL

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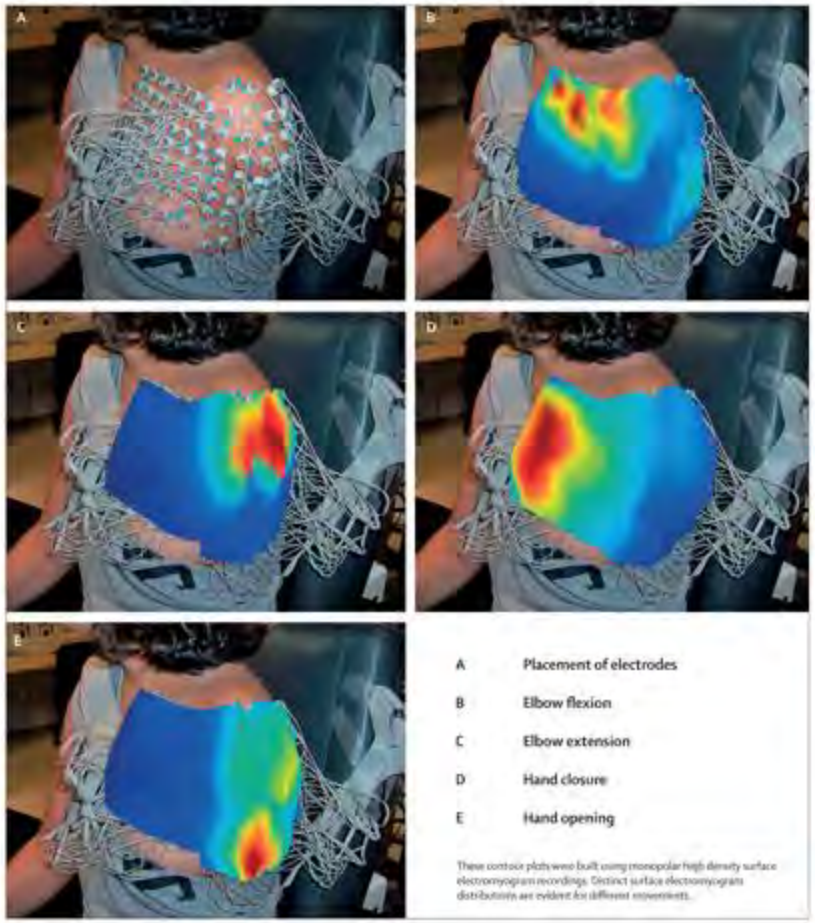

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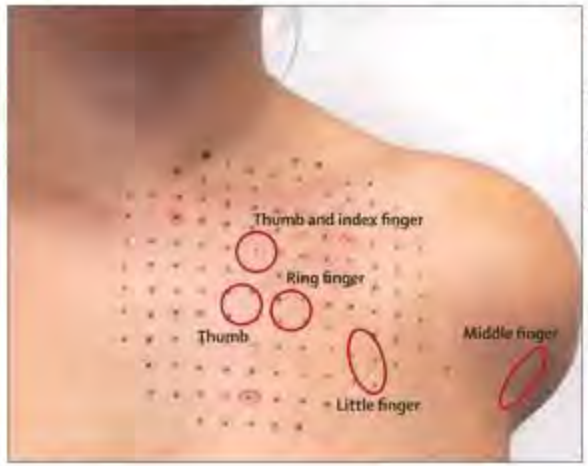

Kuiken, T. A., et. al. J. Lancet. 2007, 369, 371-380.

CORTICAL-DEPTH DEPENDENT NEUROVASCULAR RESPONSE AFTER SUBARACHNOID HEMORRHAGE

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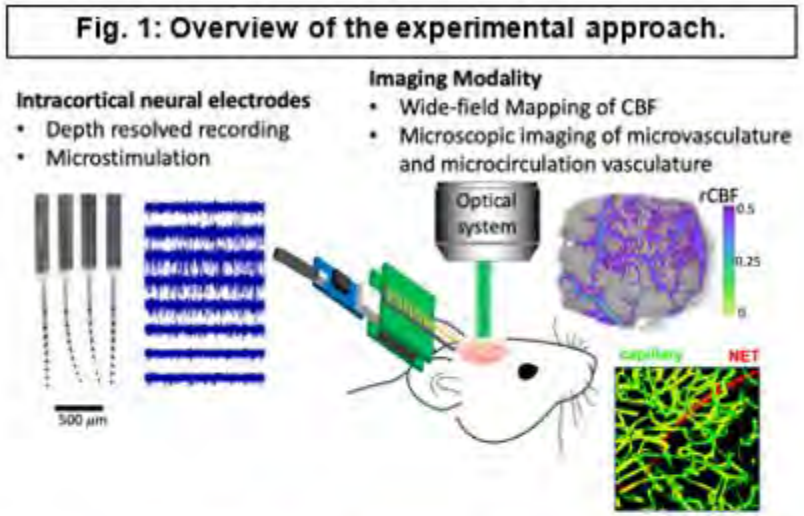

Fig. 3: NET enabled multimodal neural platform. A,B: Sketch and photo showing a chronic optical window mounted atop a NET array. **C,** *In vivo* 2P imaging at 200 µm deep showing the normal density and a intact BBB in the microcapillary (green) surrounding a NET (red). Image taken 2 months after NET implantation. Right: Matrix of line scans showing movement of red blood cells in the capillary marked by the dashed line as dark stripes, the slope of which gives the blood flow speed.

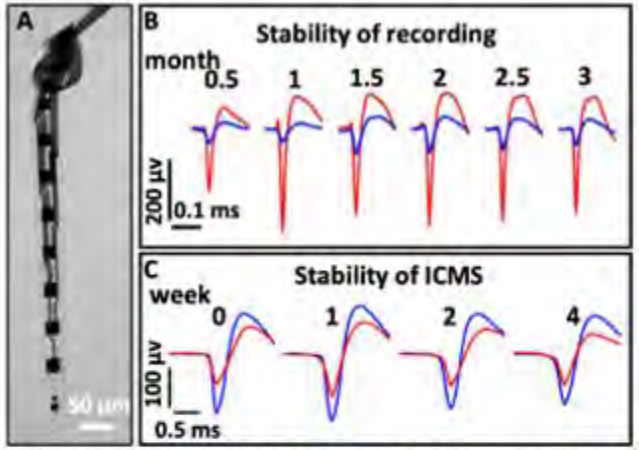

Fig. 2: NET electrodes for stable recording and ICMS. A: Ultraflexible NETs suspended in water where a knot with curvature <50 µm was made. **B**: Chronically stable recording of a single-unit action potential over 3 months. **C:** ICMS that repeatedly activated the same units (red and blue) for 4 weeks.

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The Luan laboratory of Integrative Neural Interface

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Full Research Member, Research Institute
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Houston Methodist

NEUROCOGNITIVE ABNORMALITIES FOLLOWING SAH, COMPLEMENT ACTIVATION AND NEUROINFLAMMATORY RESPONSE

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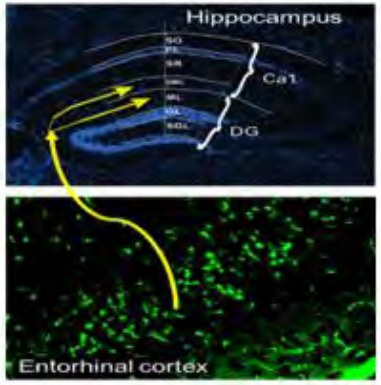

Fig.1. Upper panel. Dorsal hippocampus and PP projections from entorhinal cortex. CA1 – cornu Ammonis 1; DG- dental gyrus; SO – stratum oriens; PL – pyramidal layer; SR stratum radiatum; SLM – stratum lacunosum moleculare; ML molecular layer; GL – granular layer; SGL – subgranular layer; (4x, DAPI staining). Yellow arrows – PPs. Lower panel: Entorhinal cortex, damaged neurons stained with FJC.

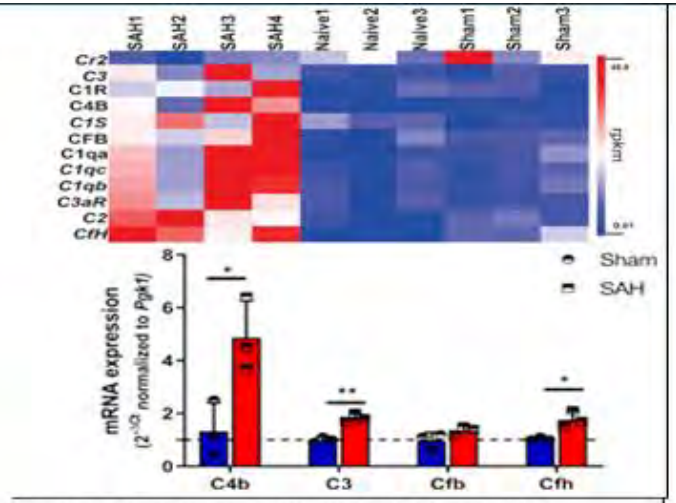

Fig. 4. Gene expression analysis of post-SAH hippocampi. (A) Heatmap of complement gene expression in SAH, Sham and Naïve hippocampi. The values of reads per kilobase of exon model per million (RPKM). (B) RT-qPCR validation of gene expression increase after SAH as compared to Sham. Data are means ± SD. *p<0.5, **p<0.01.

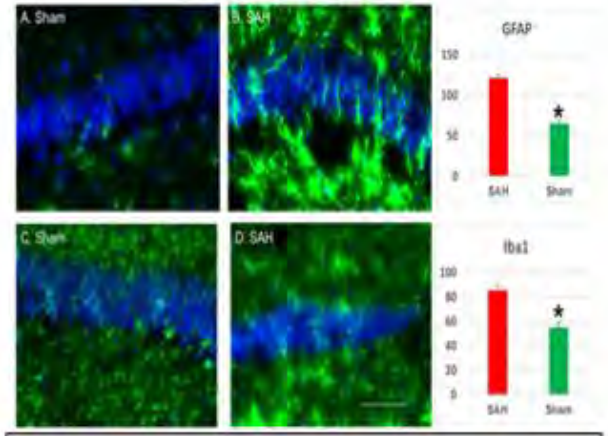

Fig. 5 Gliotic response in the DG hippocampal area following SAH. Astrocytic (green) response – top row; microglial (green) response – bottom row. Blue – DAPI (20x, bar 100 μm and respective changes in fluorescence intensity in the right column (p<0.01, n=4/group).

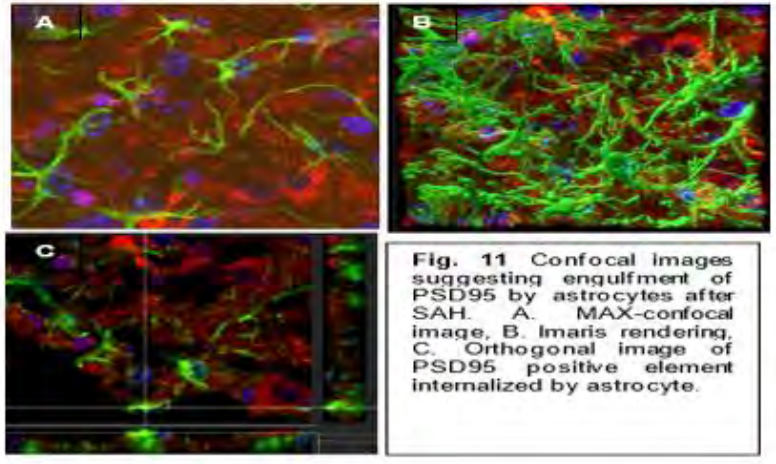

Fig. 11 Confocal images suggesting engulfment of PSD95 by astrocytes after SAH. A. MAX-confocal image, B. Imaris rendering, C. Orthogonal image of PSD95 positive element internalized by astrocyte.

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Behnaam Aazhang

J.S. Abercrombie Professor, Electrical and Computer Engineering

Director, Rice Neuroengineering Initiative

Rice University

DEVICE FOR STROKE, SAH, MTBI

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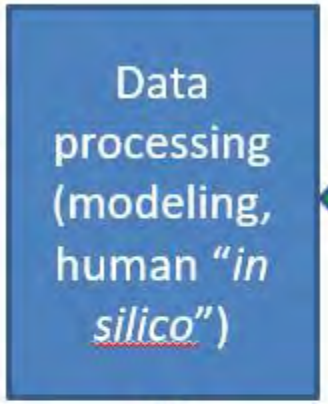
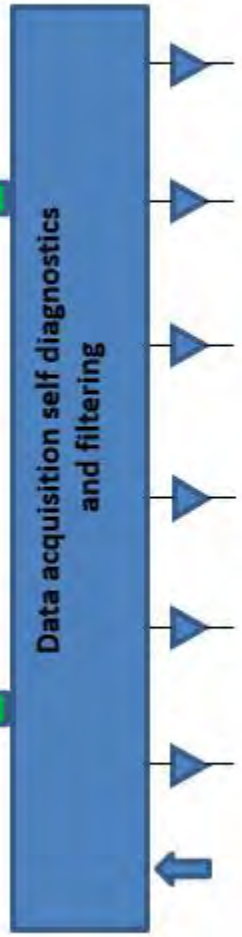
Human interface





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PGY-5

Ryan Austerman, MD
Keck School of Medicine of the University of Southern California

Texas A &M Burroughs Wellcome Fund

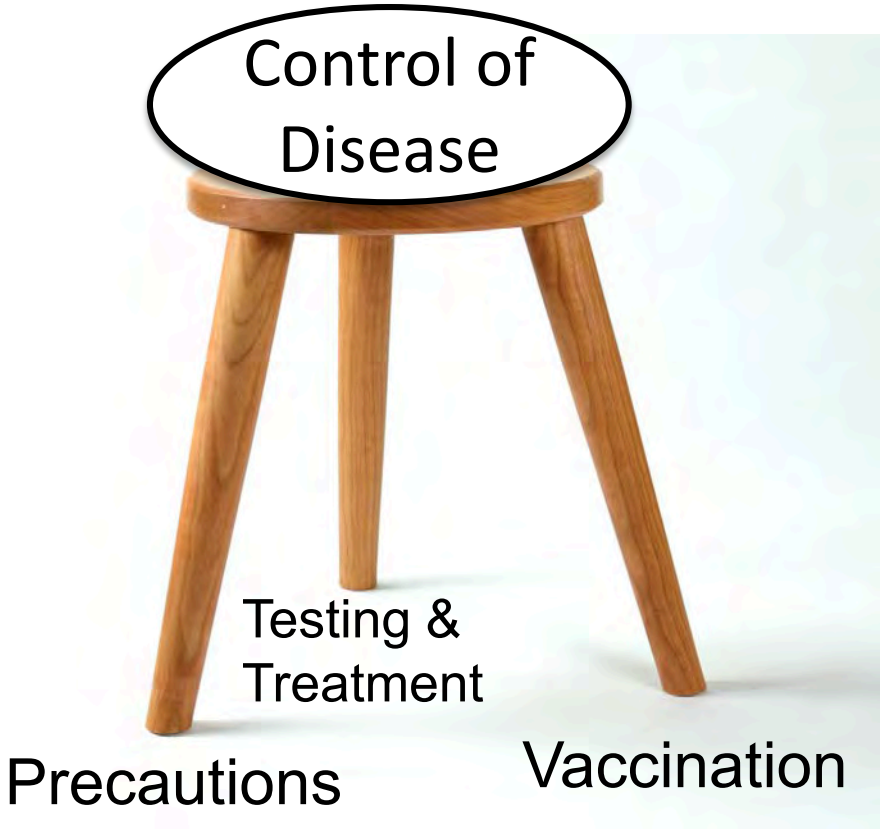
COVID-19 Updates

H. Dirk Sostman, MD FACR

Town Hall October 14, 2020

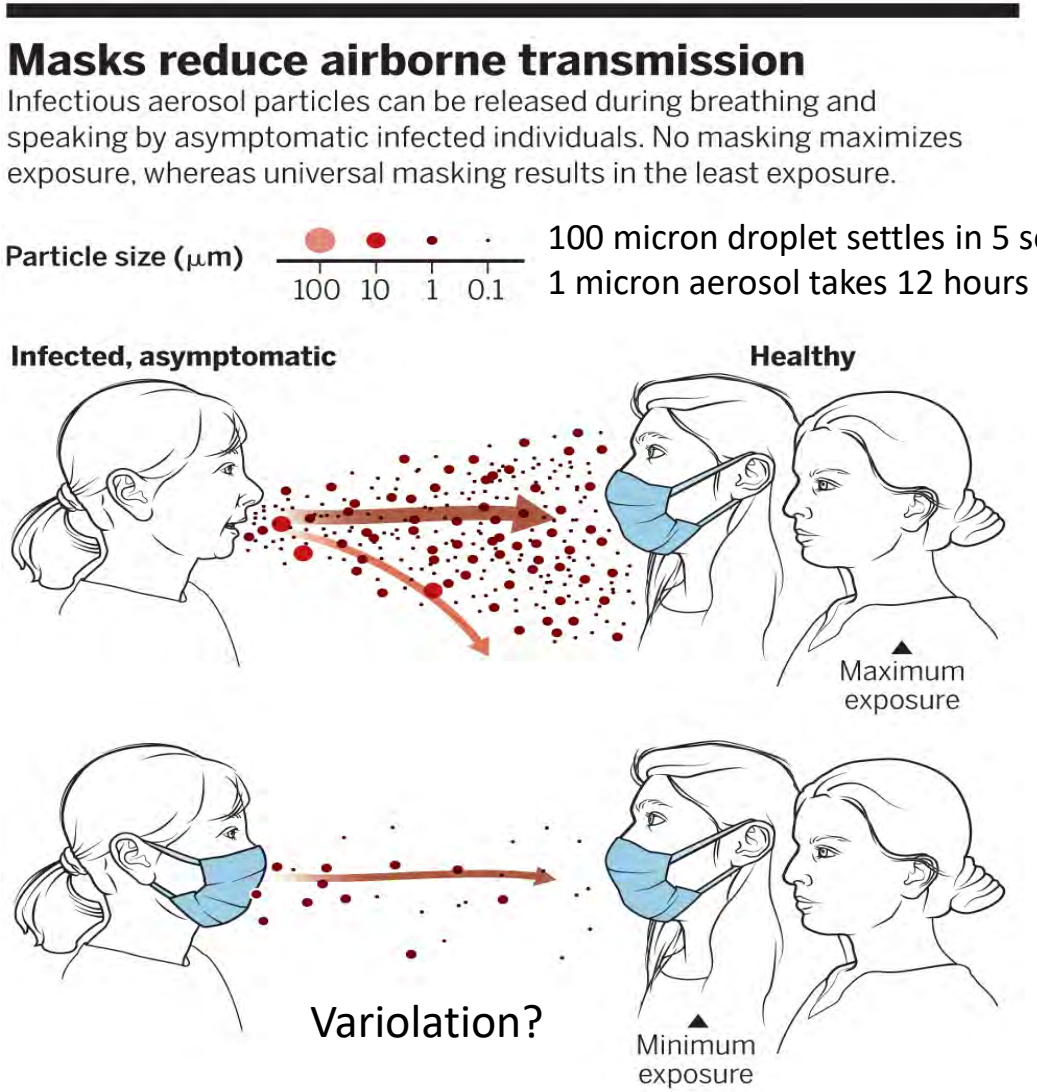
HOUSTON Methodist
LEADING MEDICINE

Controlling Infectious Diseases



Masks

Masks work!



- Misconceptions
  - Masks do not work
    - Masks protect healthy people from infected people!
    - Reduce egress / ingress of infected droplets and aerosols
  - The virus is smaller than the pores in the mask
    - Droplets are larger than pores
    - Aerosols are trapped by other mechanisms
  - Masks restrict oxygen supply
    - Measurements show no effect on oxygen or carbon dioxide
  - Masks are not needed with social distancing
    - Wrong! Sneezes and coughs can travel 30 feet
  - Masks are not needed outdoors
    - The risks are lower outdoors but transmission still possible
    - Use your judgement

Eye Protection

Can be helpful

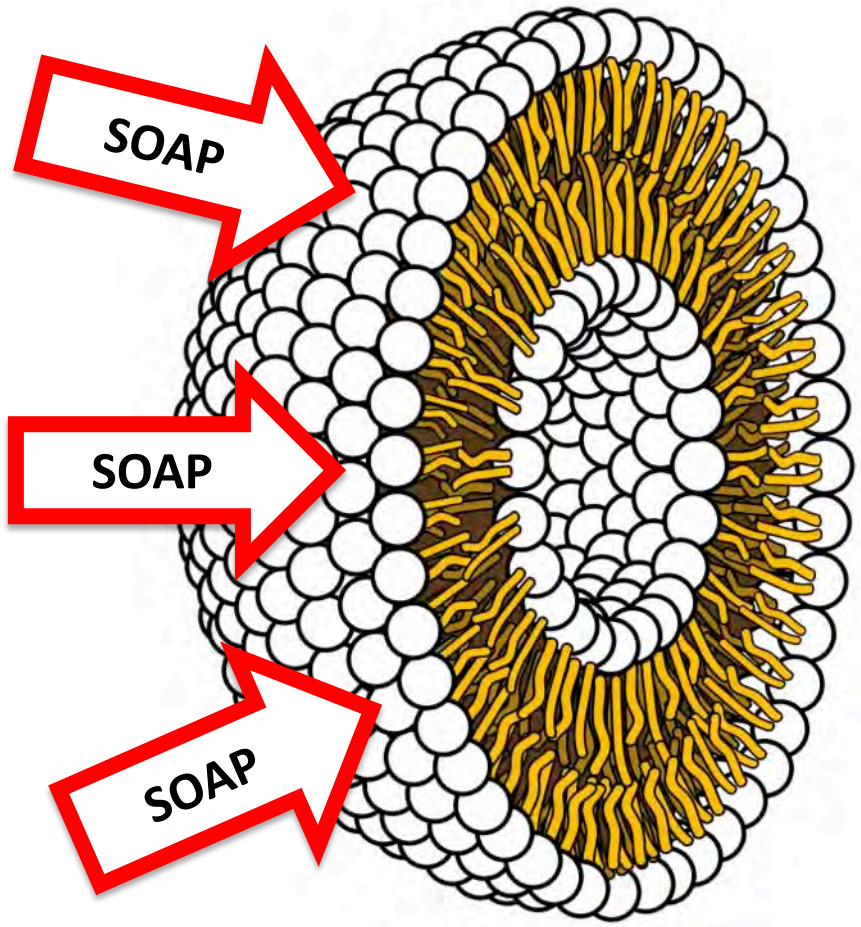
- Viruses can enter the body through the eyes
- Dose usually low because of low air flow to the eyes
  - Ballistic droplets from a cough or sneeze are a high risk
  - In high risk situations like airplanes, eye protection is recommended
- Not a substitute for masks
  - Masks protect your nose and mouth
  - Eyewear protects your eyes

$12 from Amazon

$4 from Home Depot

Handwashing

Your Mom was 100% correct



- Washing your hands with soap and water dissolves the lipid coating of the virus and inactivates it
- Alcohol-based sanitizer (60-95% alcohol) also works
- More effective to wash hands often than to try to disinfect packages, etc.

Respiratory Viruses Prosper in Winter

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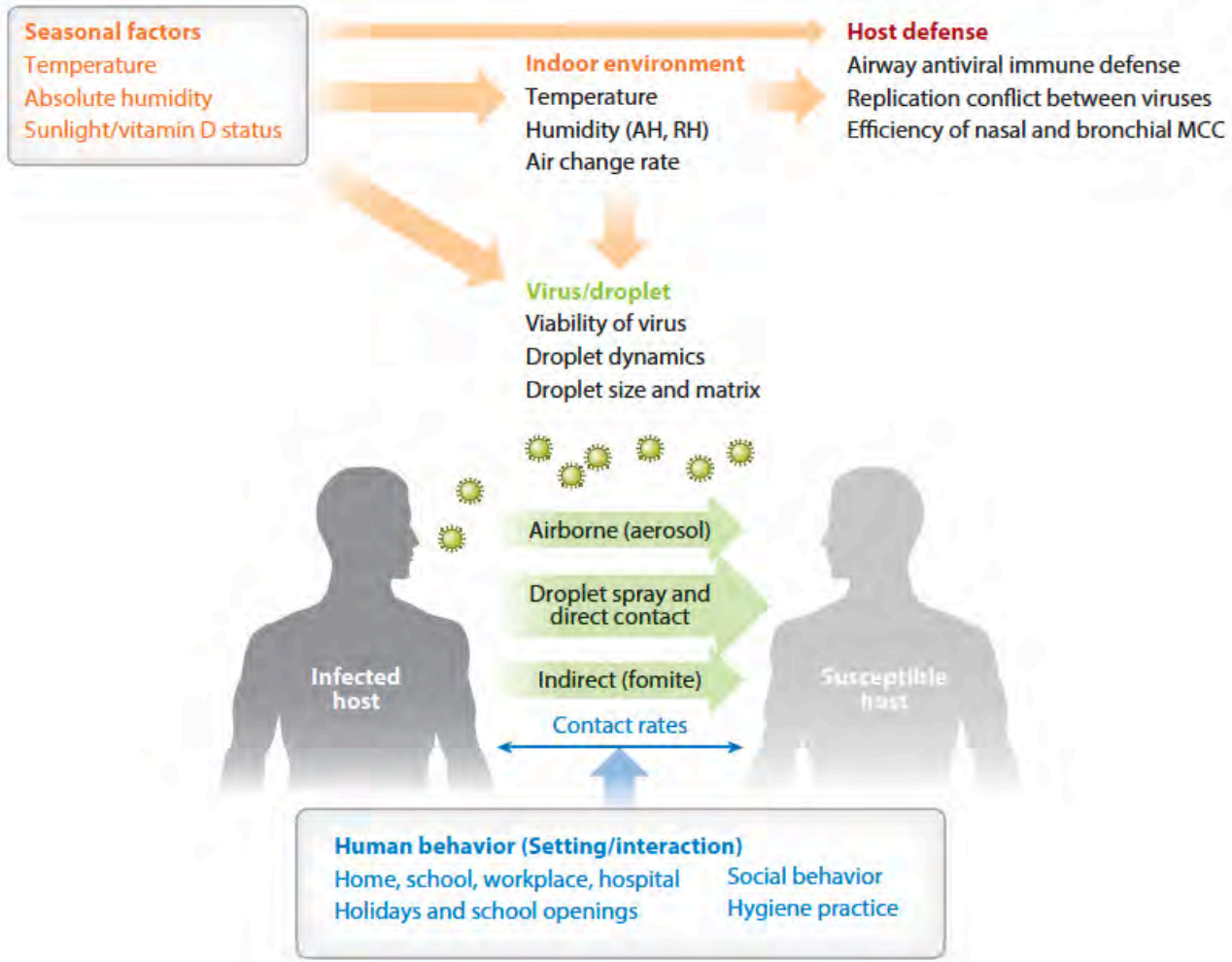
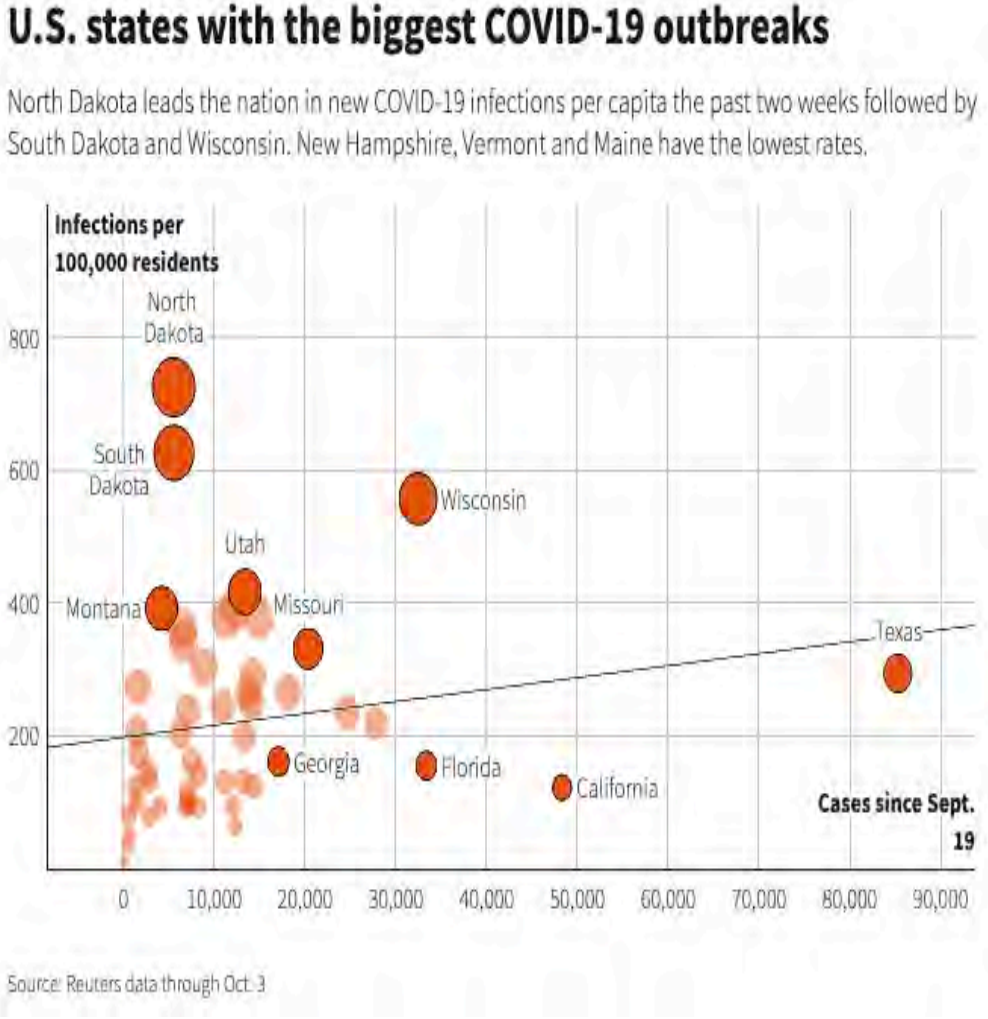
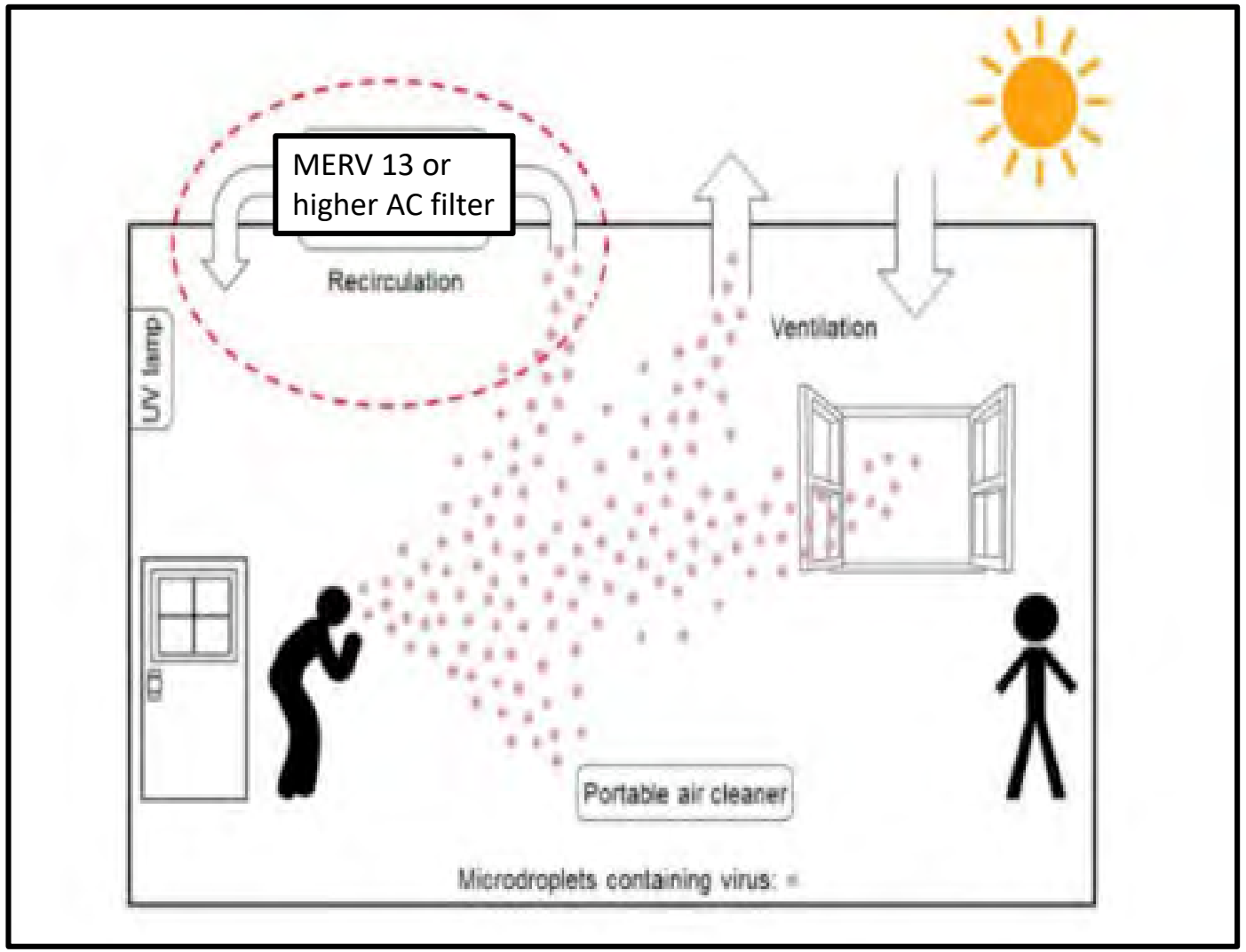




COVID-19 Winter Tips

Air Filters & Ventilation



Portable air cleaner with HEPA filter

https://tinyurl.com/FAQ-aerosols

COVID-19 Winter Tips

Temperatures & Humidity

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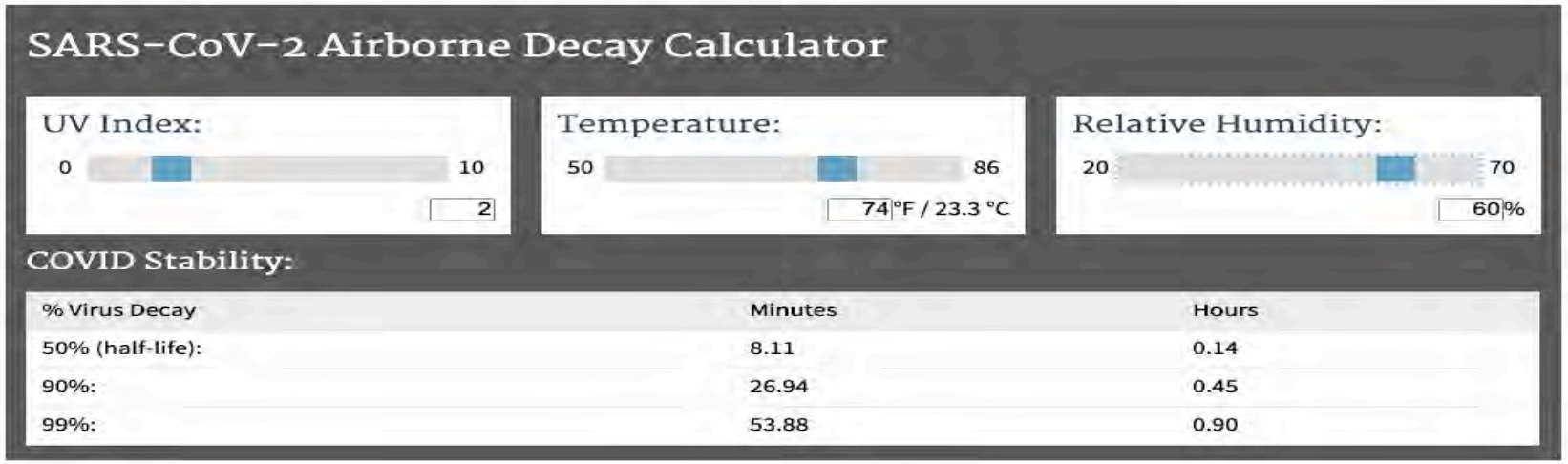
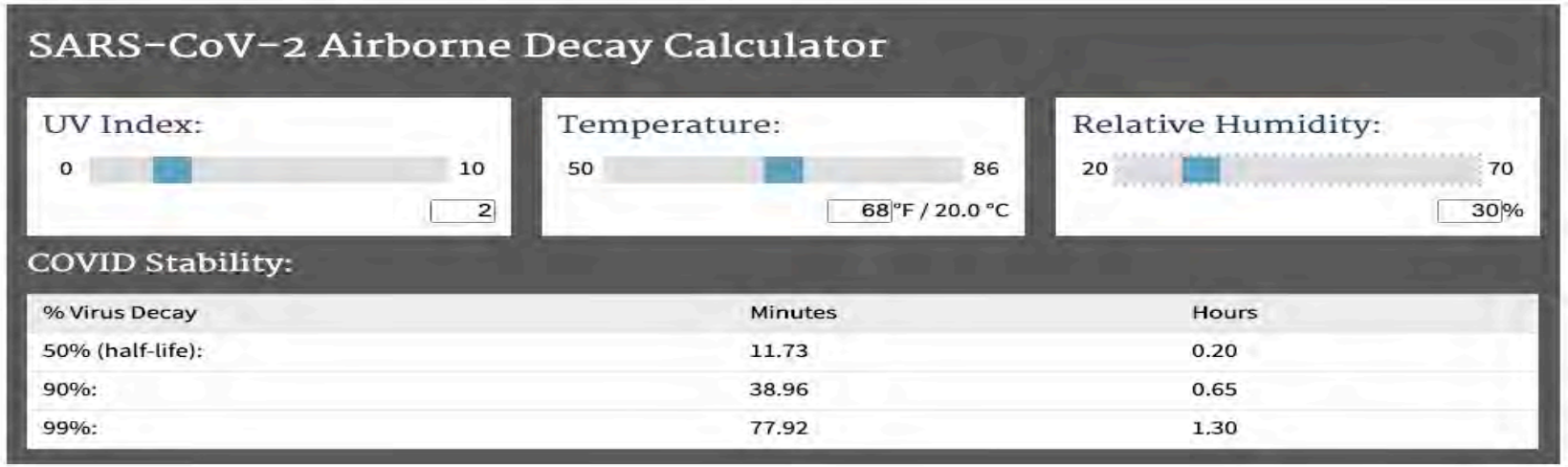


Higher RH
Higher Temperature
Reduces virus survival time



Low RH
Low Temp

https://www.dhs.gov/science-and-technology/sars-airborne-calculator

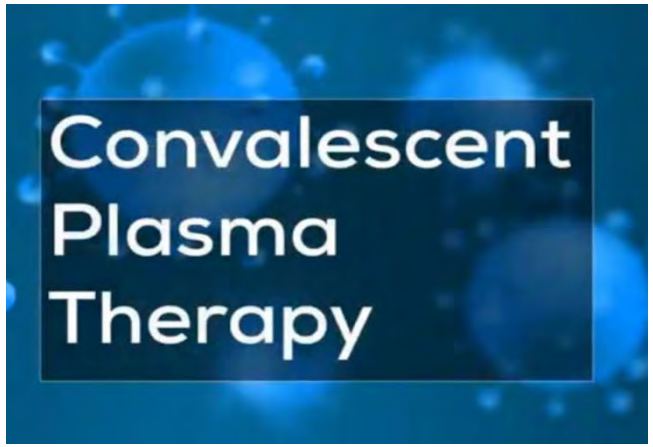
COVID-19 Winter Tips

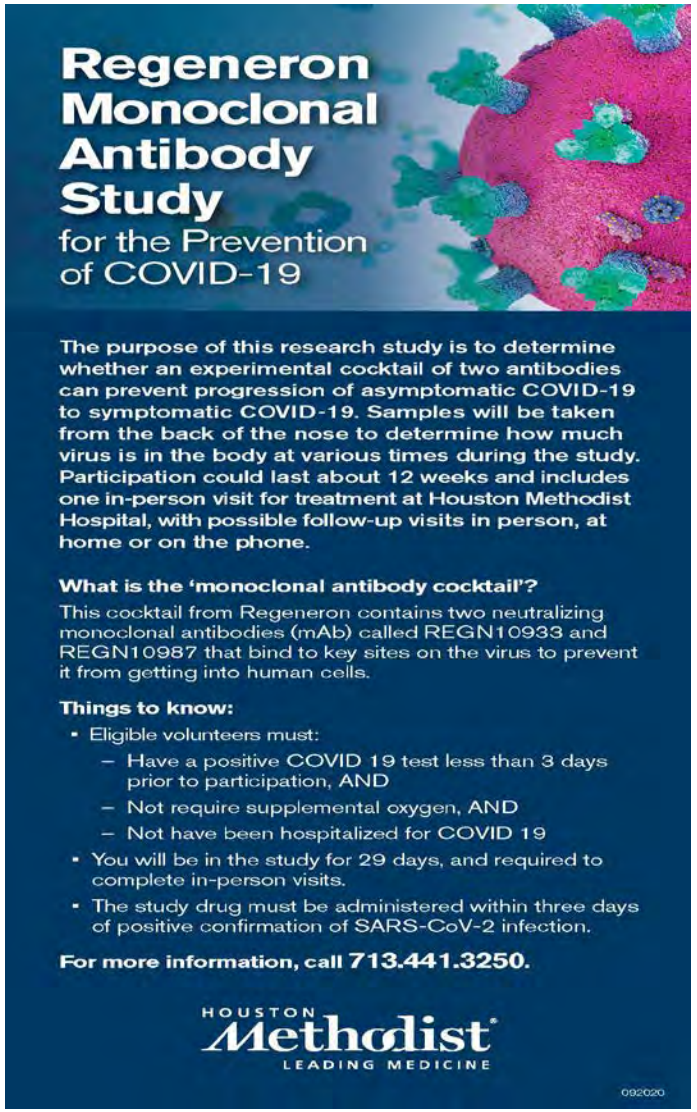
- Follow normal precautions with extra care
- Treat indoor air
  - Humidify indoor air (50% relative humidity at 70–75 F)
  - Ventilation of indoor air
  - Air filters for indoor spaces
- Wear face mask to keep nose warm and moist
- Vitamin D supplements if levels low
  - Irish Med J April 2020
  - Meltzer et al, JAMA September 2020
  - Maghbooli et al, PLOS One September 2020
  - Kaufman et al, PLOS One September 2020
- Get extra sleep
- **Get your flu shot!**

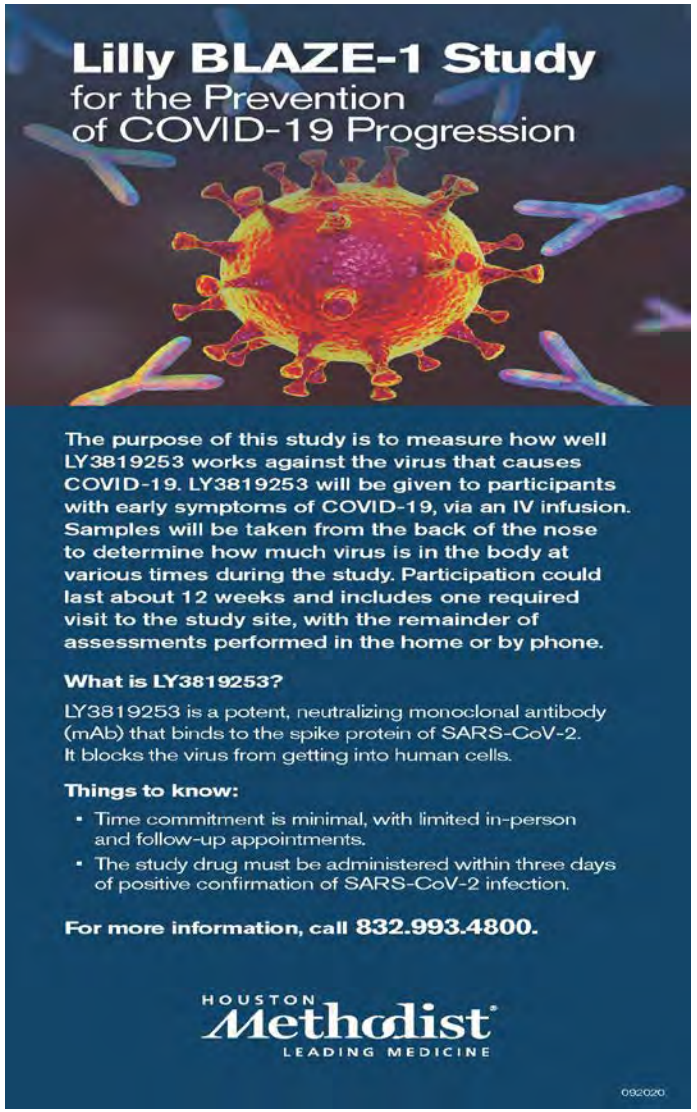
Progress in Treatments for COVID-19

Patient Group	"Proven" Effective (RCT or many cohort trials)	"Probably" Effective (still under investigation)
Outpatients	Remdesivir Convalescent plasma	Monoclonal antibodies Colchicine Favipiravir
Inpatients (including needing oxygen)	Remdesivir Convalescent plasma Baricitinib Steroids	Monoclonal antibodies Tocilizumab
Severely Ill (including mechanical ventilation & ECMO)	Steroids Remdesivir	Tocilizumab

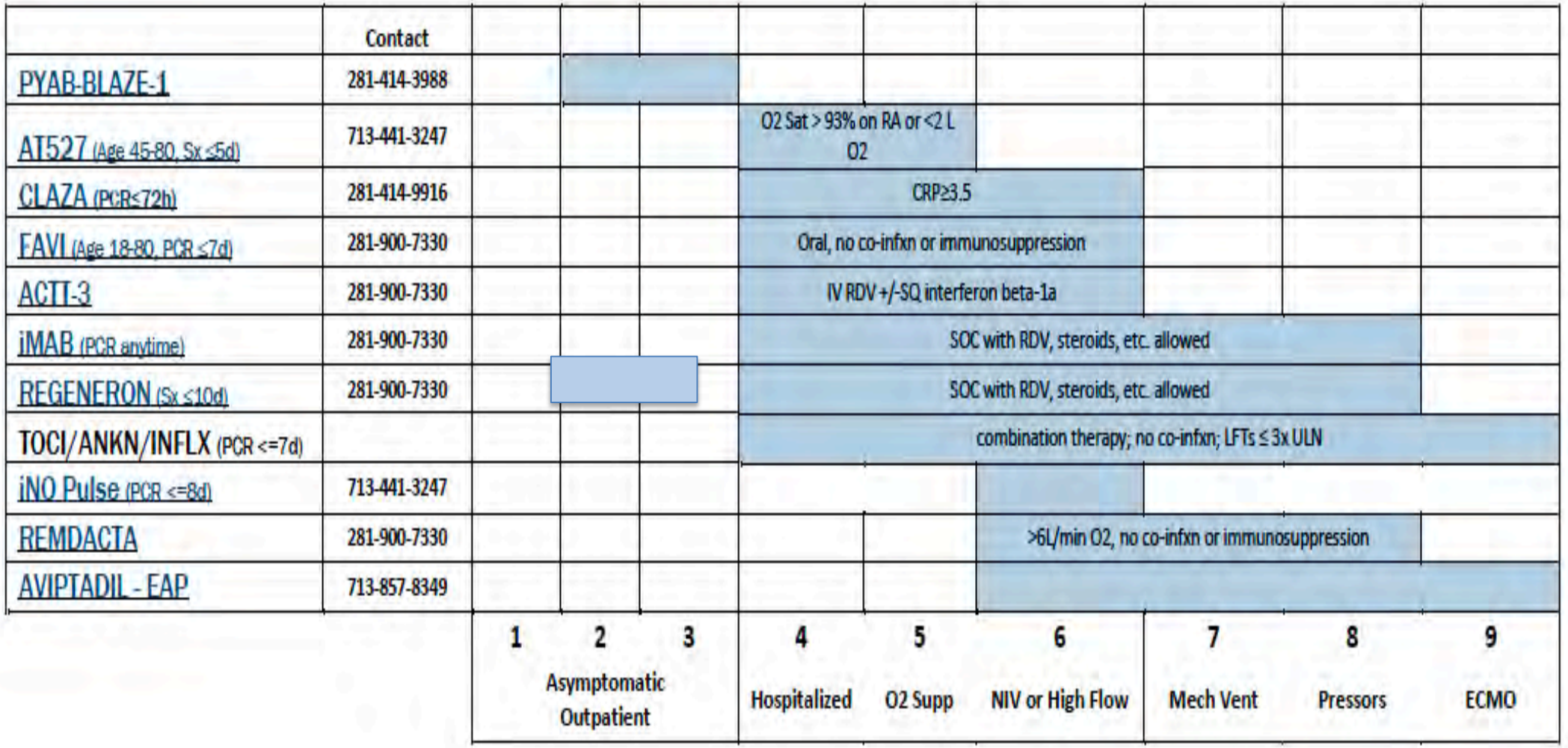
Houston Methodist Clinical Trials 2020







Houston Methodist Clinical Trials Overview



VACCINE UPDATE

HOUSTON Methodist
LEADING MEDICINE

Vaccine Progress – Immune Responses

HOUSTON Methodist LEADING MEDICINE

Vaccine	Antibody Response	T Cell Response	Species	N of Doses	Protection (Monkeys)	EUA Target
Moderna	100% (2x – 8x CP)	100%	Human	2	Infection	December 2020
Pfizer / BioNTech	100% (5x – 30x CP)	94%	Human	2		October 2020
J & J	100%	82%	Human	1	Infection	Q1 2021 **PAUSED**
Oxford / Astra Zeneca	100% (= CP)	100%	Human	2	Disease	September 2020 **PAUSED** in USA
Novavax	100% (2x CP)	100% (subgroup)	Human	2		December 2020
Inovio (MERS)	94%	71%	Human	3		??

CP = convalescent plasma

Other Vaccine Challenges

- Reluctance to accept vaccination
  - Politics, concern about side effects
- Logistics Challenges
  - Supplies (borosilicate glass vials, etc.)
  - Cold chain of refrigeration
  - Air freight capacity (8,000 jumbo jets)
  - Paperwork, customs, health regulations, etc.
  - Organizing administration, records, etc.
  - Monitoring safety, side effects

Vaccine Scenarios

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GOOD

- Scenario 1 (15%)
  - Vaccine 80%–90% effective, minor side effects
  - EUA in Q4 2020
  - Widespread vaccination in Q1 & Q2 2021
  - Would control pandemic severity
- Scenario 2 (70%)
  - Vaccine 60%–70% effective, minor side effects
  - EUA in Q4 2020
  - Widespread vaccination in Q1–Q3 2021
  - Best if paired with testing, treatment, precautions
  - Will COVID-19 eventually become milder, seasonal illness?

NOT GOOD

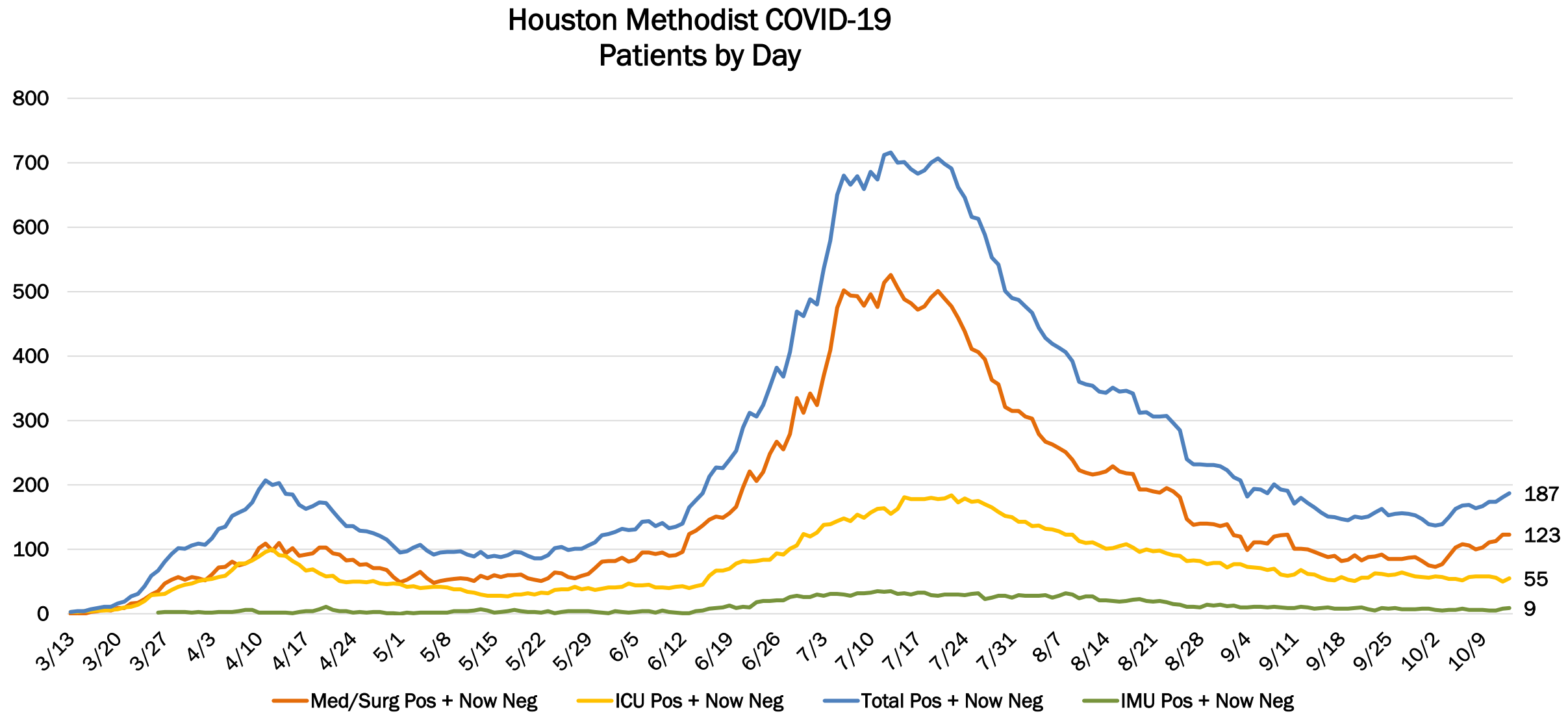
- Scenario 3 (10%)
  - Vaccine < 50% effective
  - Need to wait for next generation of vaccines (6-12 months)
  - Need to rely on testing, treatment, precautions
- Scenario 4 (< 5%)
  - Vaccine has serious side effects
  - Need to wait for next generation of vaccines (> 1 year)
  - Safety testing will take **much** longer
  - Need to rely on testing, treatment, precautions

COVID-19 Update

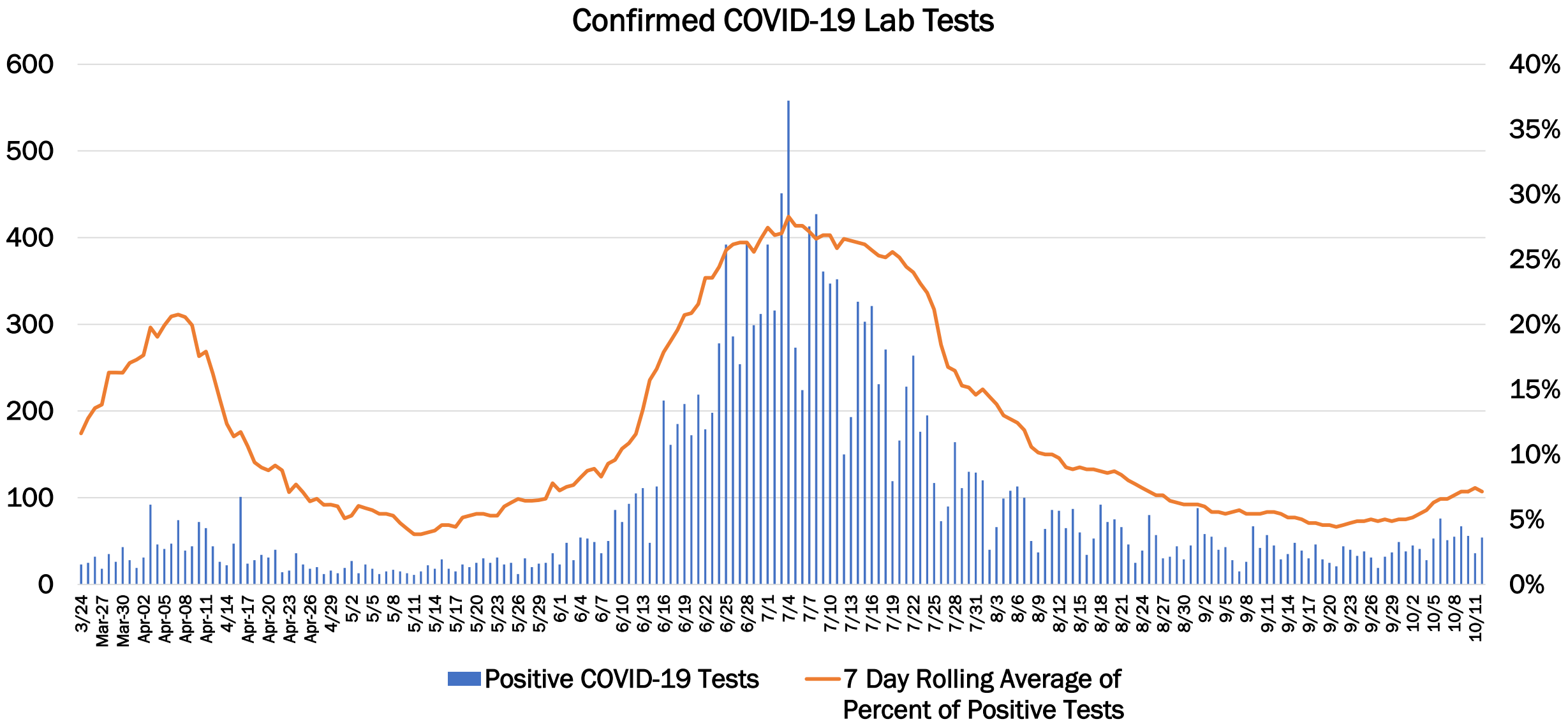
October 14, 2020

HOUSTON Methodist LEADING MEDICINE

Houston Methodist COVID-19 Cases by Day



Houston Methodist Testing Trend



Houston Area Rt Estimate Trend

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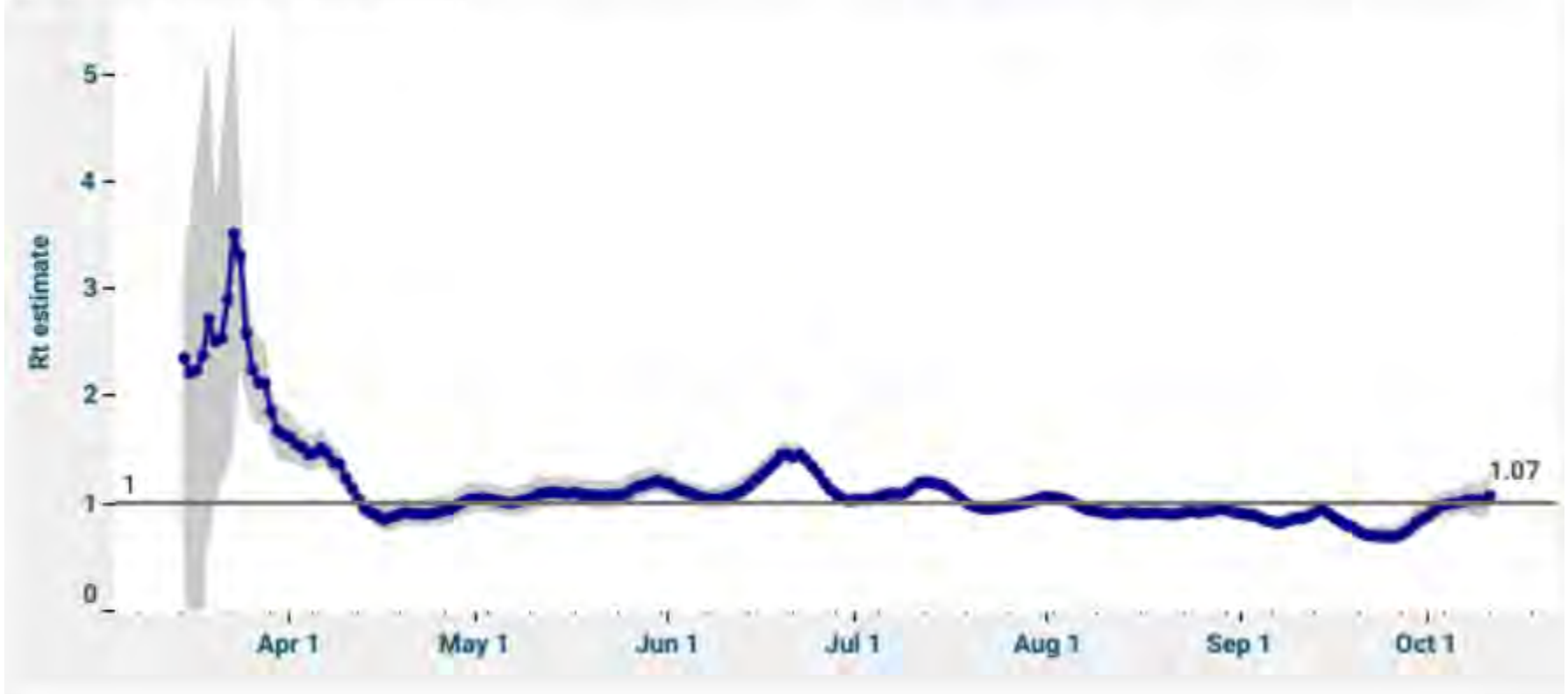
Rt estimate

This graph shows the R(t) over time. R(t) is a measure of contagiousness or how many people one COVID19 person infects. If R(t)>1, the epidemic is increasing. If R(t)< 1, the epidemic is declining. There is higher alert if the whole interval is above the horizontal line at 1. For **Q - Houston**, the rate of contagiousness is **1.07**; the epidemic is **increasing**.



https://sph.uth.edu/dept/bads/covid19-dashboard; similar BCM site: https://ictr.github.io/covid-19-county-R0/

How long do you anticipate us needing to continue with mitigating activities for COVID-19 and what is the probability for another pandemic in the near- to mid-term future?

When will life be totally back to normal or will it ever be ?

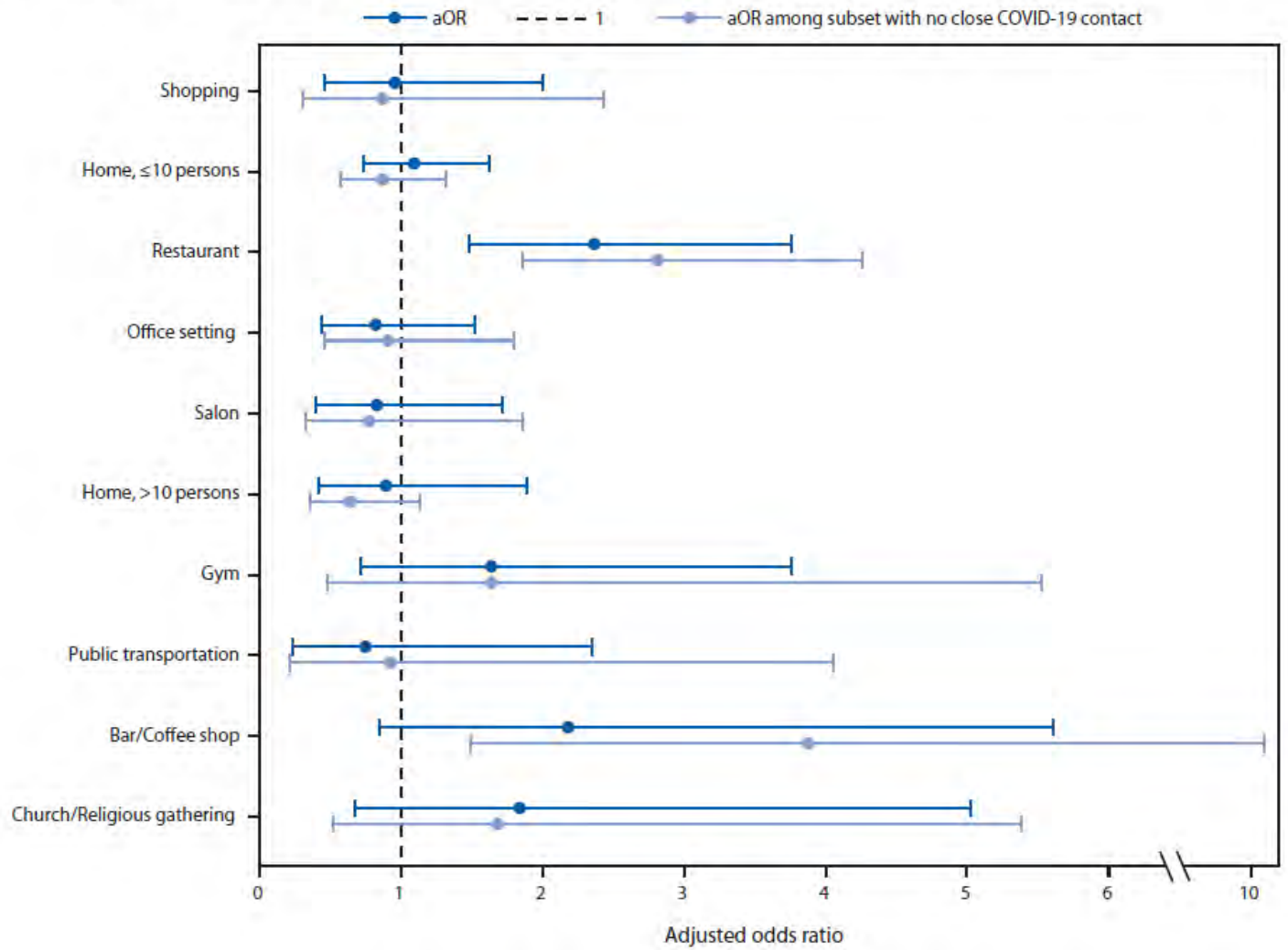
When is it safe to come out again?

Now that the COVID situation in Houston is improving, what advice do you have on how we should continue to live? For example, for someone between 45-55 years old, is it now relatively safe to eat outdoors at a restaurant? At a friend's house? If not, when would you consider it to be safe?

If someone is eating outside at a restaurant in close proximity to someone who had COVID for two days and now has no symptoms and is not quarantining, and has decided to go out to eat, what are the chances of the non-infected person getting COVID from the person who has not quarantined for the proper duration?

Close Contact Exposures Associated with COVID-19

FIGURE. Adjusted odds ratio (aOR)* and 95% confidence intervals for community exposures† associated with confirmed COVID-19 among symptomatic adults aged ≥18 years (N = 314) — United States, July 1–29, 2020



https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6936a5-H.pdf

"...going to locations that offer on-site eating and drinking options were associated with COVID-19 positivity. Adults with positive test results were approximately twice as likely to have reported dining at a restaurant than were those with negative test results."

Also, we pass people closely on the street when walking our dog. Is that ok without a mask?

COVID-19 Precautions

Make trick-or-treating safer

- Avoid direct contact with trick-or-treaters.
- Give out treats outdoors, if possible.
- Set up a station with individually bagged treats for kids to take.
- Wash hands before handling treats.
- Wear a mask.

https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/holidays/halloween.html

Is an endoscopy safe? I don't want to take my mask off. How do I know it isn't in the air in the procedure room?

Delay and Avoidance of Preventive and Screening Medical Care

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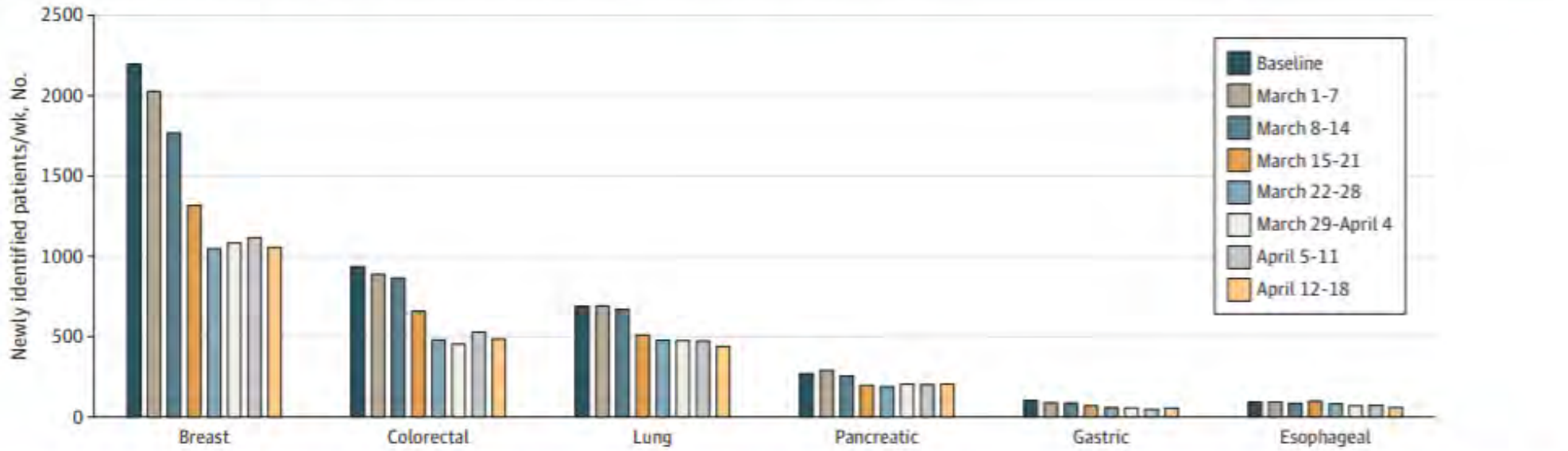
JAMA Network | Open

Figure. Newly Identified Cancers, Baseline Mean and Weekly During the Coronavirus Disease 2019 Pandemic



"...the mean weekly number of new diagnoses for six common cancers dropped by 46%, with breast cancer diagnoses declining the most (52%), in March and April compared to the two months prior."

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768946

How is Houston Methodist doing?

Goals for the New Normal – May

1. Houston Methodist will be the safest hospital system in the world
2. Volumes will be back to normal by July 1
3. Achieve at least breakeven by the end of the year
4. Maintain full operations during a second surge
5. Avoid furloughs, layoffs, and pay cuts

These goals will be the guiding principles for ongoing decision making during this transition to the new normal. We will continue to adjust these goals as circumstances change.

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These goals will be the guiding principles for ongoing decision making during this transition to the new normal. We will continue to adjust these goals as circumstances change.

Goals for the Remainder of 2020

1. Houston Methodist will be the safest hospital system in the world
2. Volumes will again be back to normal by October 1
3. We will achieve ~75% of budgeted operating margin for September – December
4. Maintain full operations throughout the COVID pandemic
5. Press our strategic advantage

Houston Methodist will use these guiding principles in decision making and goal setting. We will remain nimble and adjust these goals as circumstances change.

Press Our Strategic Advantage

1. Focus on unparalleled safety, quality, service and innovation

U.S. News & World Report

- On the Honor Roll – Ranked #20 in the country
- Houston Methodist Hospital is ranked for the 28th consecutive year in at least one specialty
- Named No. 1 in Texas nine years in a row
- Received “High Performing” in 10 out of 10 of the procedures & conditions
- For the 14th consecutive year, Houston Methodist Hospital ranked in more specialties than any hospital in Texas

- Ranked in 11 of 16 specialties:
  - Cancer (#17)
  - Cardiology & Heart Surgery (#12)
  - Diabetes & Endocrinology (#28)
  - Ear, Nose & Throat (#49)
  - Gastroenterology & GI Surgery (#14)
  - Geriatrics (#26)
  - Gynecology (#26) *tied with UCLA*
  - Nephrology (#19) *tied with Duke*
  - Neurology & Neurosurgery (#23)
  - Orthopedics (#13)
  - Pulmonology and Lung Surgery (#20)

Unparalleled Safety and Quality

Vizient Quality & Accountability Results 2020

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	Academic	Specialized Complex Care	Complex Care				Community
	HMH	HMSL	HMB	HMW	HMWB	HMTW	HMCL
Overall	6	2	17	7	8	5	53
Mortality	1	1	9	15	24	17	32
Efficiency	37	32	47	19	27	48	113
Safety	7	1	12	9	2	1	39
Effectiveness	47	53	77	3	44	51	101
Patient Centeredness	47	16	59	33	28	29	95
Star Rating	★★★★★	★★★★★	★★★★	★★★★★	★★★★★	★★★★★	★★★

Note: 2018 survey split hospitals into three categories; 2019 and 2020 survey split hospitals into four categories.
Blue is "Vizient Top Performer" or 10th percentile. Green is 10th to 25th percentile. Yellow is 25th to 50th percentile. Red is below the 50th percentile.

Press Our Strategic Advantage

1. Focus on unparalleled safety, quality, service and innovation
2. Care for our people
3. Invest strategically and aggressively in academic programs
4. Optimize marketing and public relations for further differentiation
5. Continue strategic plans for expansions and recapitalization
6. Invest aggressively in innovation

THANK YOU FOR ATTENDING OUR TOWN HALL CONVERSATION

If you would like more information about Neurology, Neuroprosthetics or The Society for Leading Medicine, please contact foundation@houstonmethodist.org

Take care and be well

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