May 21, 2021

Interagency Collaborative to Accelerate Research on Epilepsy (ICARE)

Research Updates

National Institute of Neurological Disorders and Stroke

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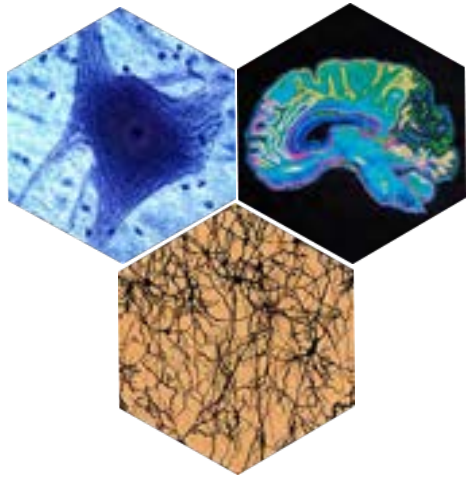
The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease



Strategies:

- Invest in basic, translational and clinical research
- Identify gaps in research and public health needs
- Train a talented and diverse research workforce
- Support development of tools and resources to enable discoveries
- Communicate and collaborate with all stakeholders, including the public
- Evaluate and continuously improve all NINDS programs

NINDS Appropriation History

(Dollars in Thousands)

	FY 2018	FY 2019	FY 2020	FY 2021 Appropriation
NINDS Base	1,776,720	1847,660	1,979,476	2,014,208
BRAIN $ to NINDS Base	111,410	111,410	128,890	178,890
21st Century Cures	43,000	57,500	70,000	50,000
HEAL	213,900	257,843	266,321	270,295
Total NINDS Appropriation	2,145,030	2,274,413	2,444,687	2,513,393

1.75% increase

2.8% increase

* These columns do not include the monies that NINDS received for the HEAL Initiative and CURES Act.

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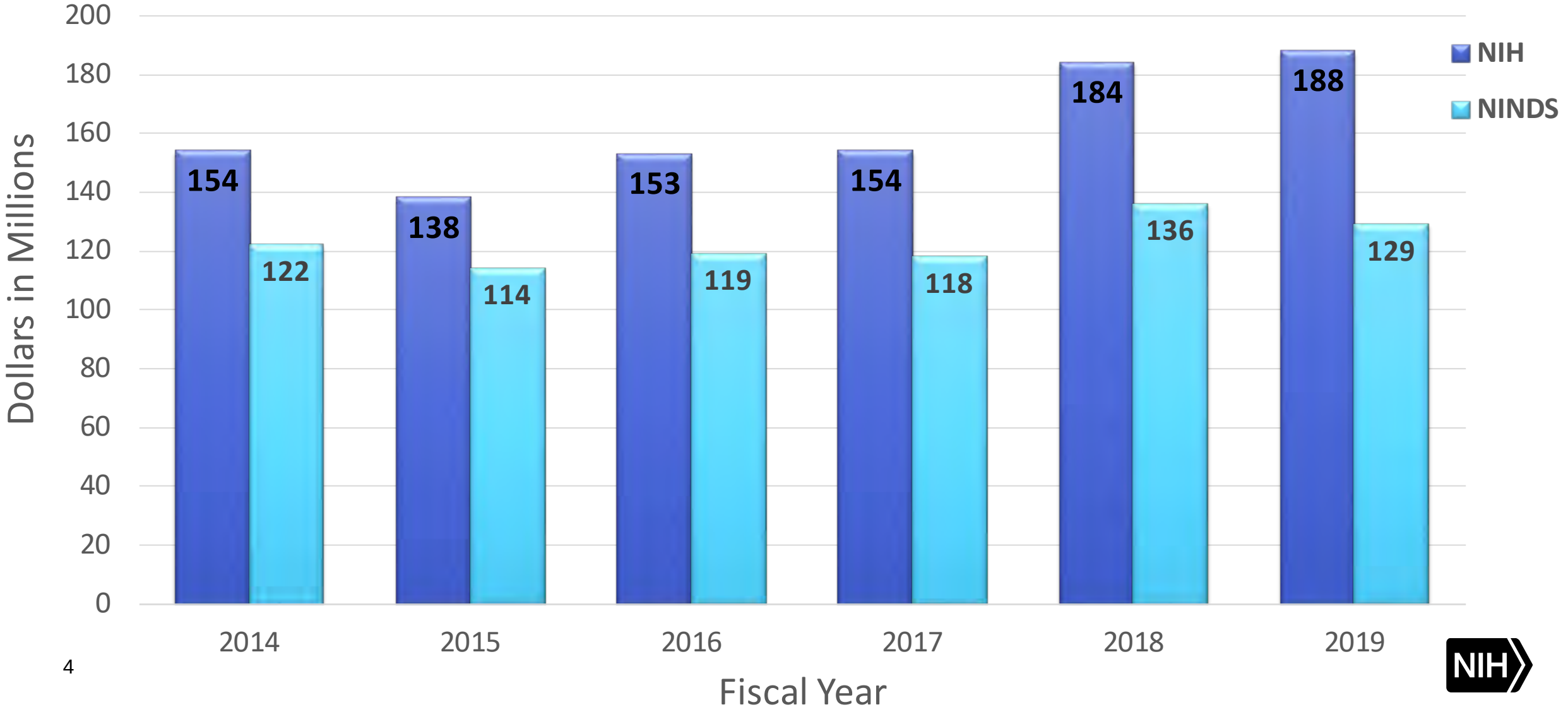
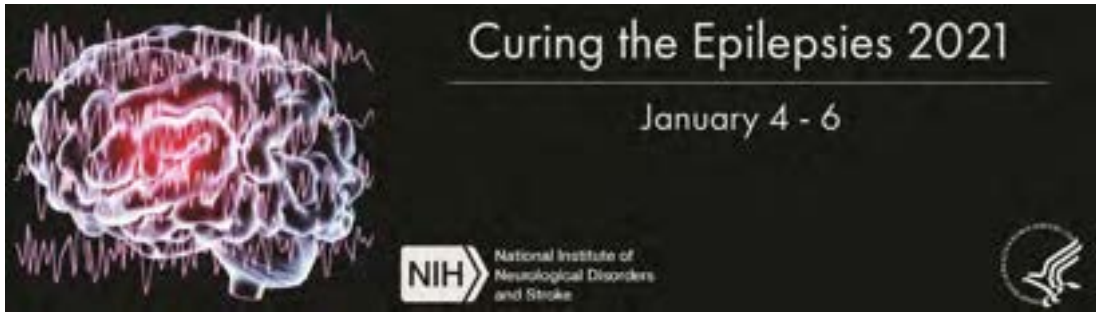
NIH and NINDS Funding for Epilepsy Research



Curing the Epilepsies: Setting Research Priorities



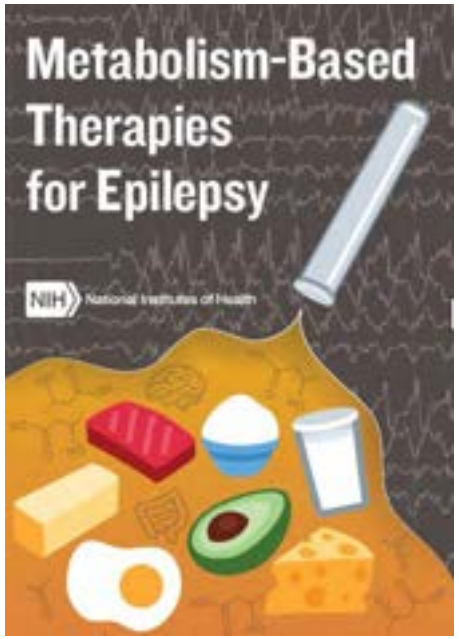
Meeting sessions can be viewed on NIH Videocast:

Day 1: https://videocast.nih.gov/watch=36065
Day 2: https://videocast.nih.gov/watch=36066
Day 3: https://videocast.nih.gov/watch=36073

This conference was an opportunity for all epilepsy research stakeholders to provide input on the transformative research priorities for the field, and to come together to find ways to move toward "Curing the Epilepsies"

- 2021 Benchmarks: The revised benchmarks will serve an important need to continue to foster a breadth of research on the epilepsies across all four Benchmark Areas
- Transformative Research Priorities: Several recurring themes were discussed throughout the conference and will continue to be the topics of ongoing discussions
  - Need to foster and support ideas and mechanisms to advance sharing and collaboration, such as a greater use of "center-without-walls" and other team science models

NINDS-sponsored Workshops on the Epilepsies



- Held November 9, 2020
- Meeting presentations can be viewed on the YouTube channel: **NIHNINDS** https://bit.ly/3kwjXvD

Post-Traumatic Epilepsy: Models, Common Data Elements, and Optimization

- Sessions are ongoing:
  March 18, April 22, May 20, and June 17, 2021
- Meeting website:

https://event.roseliassociates.com/post-traumatic-epilepsy

Joint CDC-NINDS Webinar Introduction to Health Services Research in the Epilepsies

A Joint CDC-NIH Webinar
June 9, 2021
3:30 – 5:00 pm Eastern Time

Join ZoomGov Meeting
https://cdc.zoomgov.com/j/1619474467?pwd=bWloUHRlajhhRzNQMEJuSENhaE14Zz09

Objectives:
1) To increase understanding of HSR objectives and approaches.
2) To increase understanding of how HSR can be used to close gaps in health care and management of epilepsy.
3) To increase understanding of underutilized resources for conducting epilepsy HSR studies.

NINDS Epilepsy Therapy Screening Program (ETSP)

ETSP provides preclinical screening to identify new treatments for epilepsy

- Recently approved treatments the ETSP contributed to the identification include: XCOPRI (cenobamate) and Epidiolex (cannabidiol)

The ETPS was reviewed in 2020 by a Working Group of the NINDS Advisory Council

- Key Recommendations:
  - Continue focus on identifying treatments for drug resistant epilepsy
  - Enhance capabilities to provide pharmacokinetic data
  - Expand anti-epileptogenesis/disease modification screening capabilities

ETSP Program Director - Brian Klein, PhD
ETSP contract screening site PI- Karen Wilcox, PhD

Epilepsy Centers Without Walls (CWOWs)

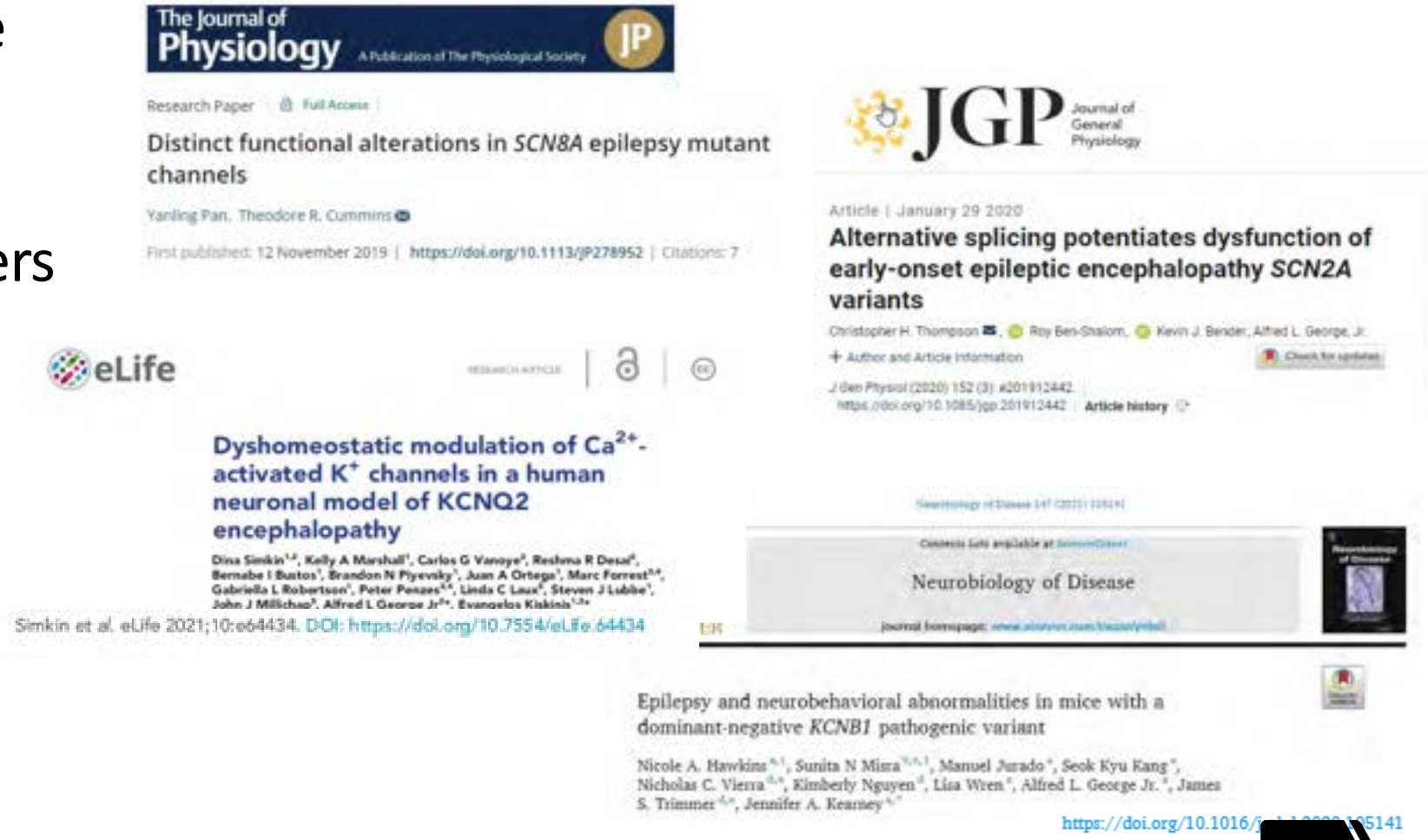
The Epilepsy Bioinformatics Study for Antiepileptogenic Therapy (EpiBiosS4Rx) will use studies of animals and patients with traumatic brain injury (TBI) leading to post-traumatic epilepsy (PTE) in order to develop future clinical trials of epilepsy prevention therapies.

The Channelopathy-Associated Epilepsy Research Center (CAERC) will combine high-throughput technologies and high-content model systems to investigate the functional consequences of genetic variants in channelopathy-associated epilepsy.

The Epilepsy Multiplatform Variant Prediction (EpiMVP) Center Without Walls will develop a modular, highly integrated platform approach to accelerate determination of the functional, pharmacological, neuronal network and whole animal consequences of genetic variants among a range of clinical epilepsy types.

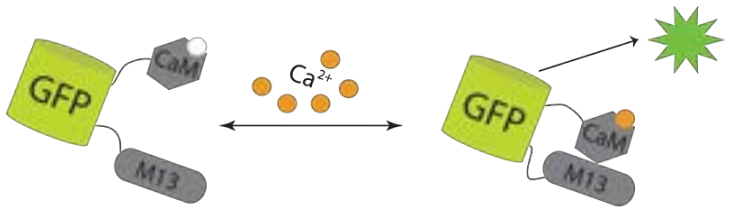
Science Advances: Functional Consequences of Genetic Variants in Channelopathy-Associated Epilepsy

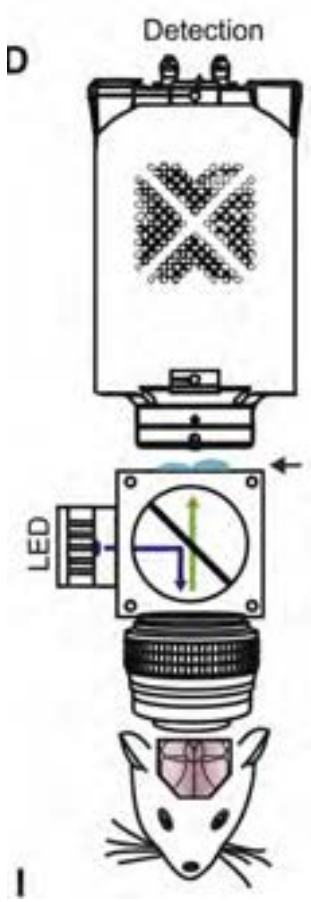
- Initial findings from the Channelopathy-Associated Epilepsy Research Center (Centers Without Walls)
- These studies suggest changes in function in variants of human epilepsy ion channels SCN2A, SCN8A, KCNQ2 and KCNB1



Tools to Explore Neural Networks Underlying Epilepsy

Florescent proteins that emit light when Ca++ enters a cell signal a firing neuron





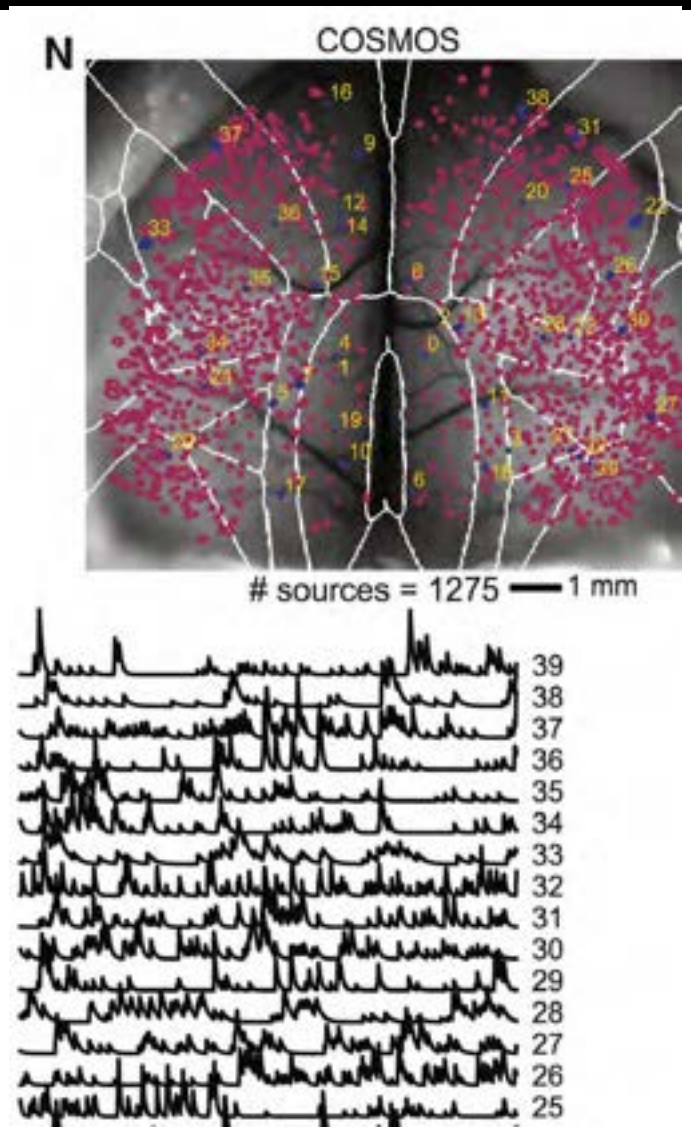
Cortical Observation by Synchronous Multifocal Optical Sampling Reveals Widespread Population Encoding of Actions

https://www.sciencedirect.com/science/article/pii/S0896627320303159

Isaac V. Kauvar,[1,2,7] Timothy A. Machado,[1,7] Elle Yuen,[1] John Kochalka,[1,3] Minseung Choi,[1,3] William E. Allen,[1,3,4] Gordon Wetzstein,[2] and Karl Deisseroth[1,5,6,*]

Neuron *107*, 351–367, July 22, 2020

Tools to Capture Neural Networks Underlying Epilepsy. Challenge of Analysis and Theory



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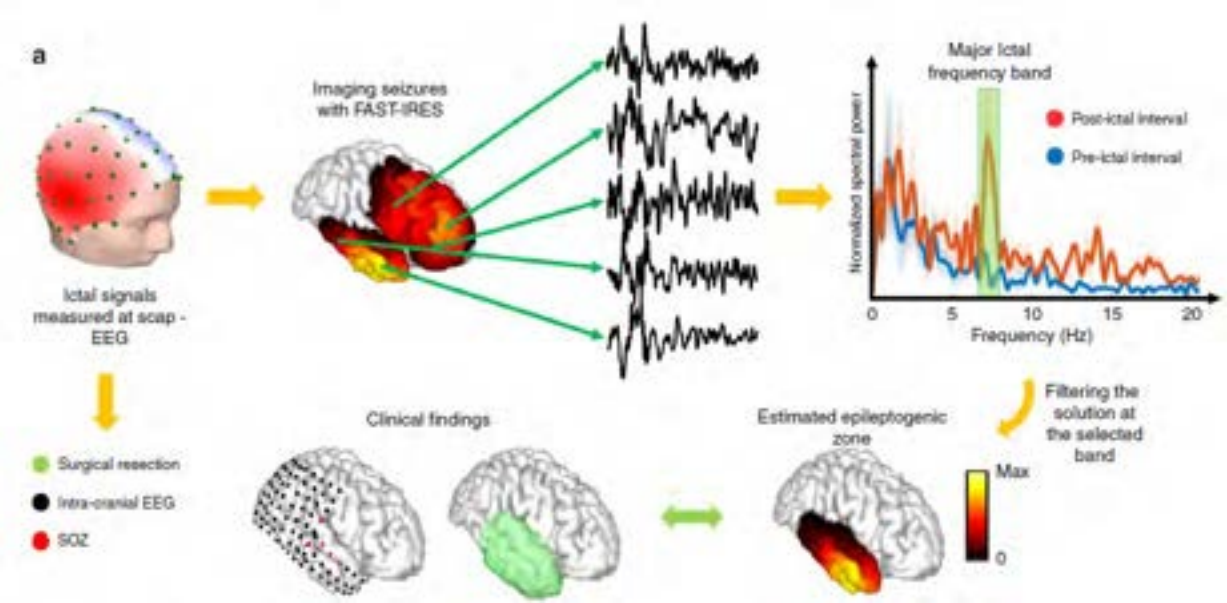
Ongoing Clinical Trials and Natural History Studies

- Preventing Epilepsy using Vigabatrin in Infants with Tuberous Sclerosis Complex (PREVeNT) Trial
- Dietary treatment of Glucose Transporter Type 1 Deficiency (G1D)
- Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD)

New Shifts in Dynamic and Noninvasive Human Brain Imaging Technology

- Dr. Gregory Worrell from the Mayo Clinic in Minnesota and his colleagues from the Carnegie Mellon University in Pennsylvania created a novel non-invasive, high-spatiotemporal resolution source imaging approach to map the brain networks of individuals with epilepsy
- FAST-IRES can work in collaboration with existing hardware to improve, for instance, the management of epilepsy

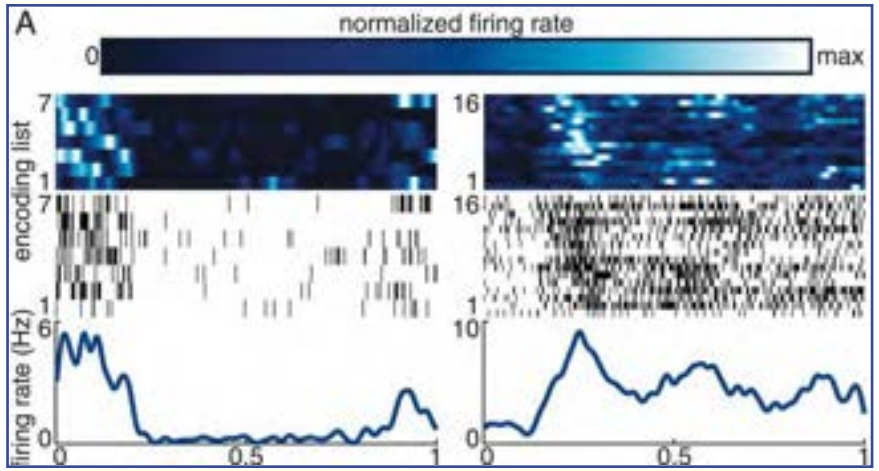


Sohrabpour et al., *Nat Communications,* 2020

People with Epilepsy are Teaching Us How the Brain Works

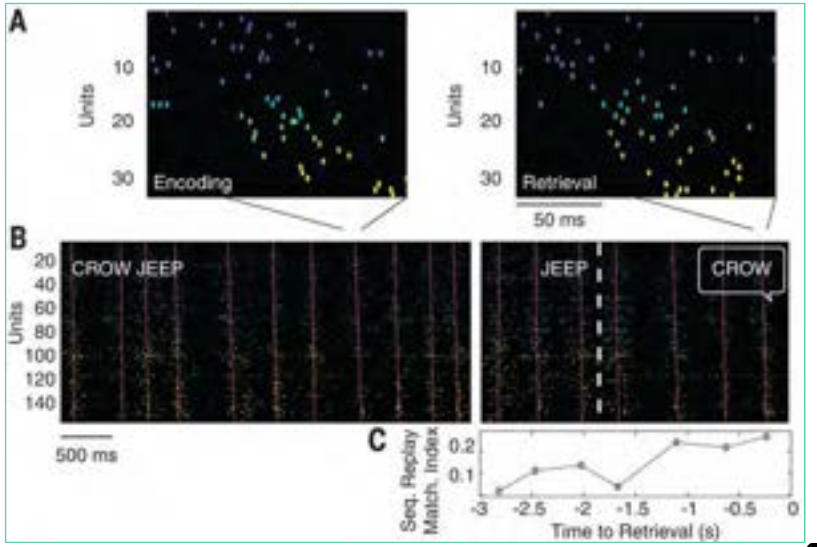
- A number of people with epilepsy who receive electrodes as part of their therapy generously volunteer for additional research on how the brain thinks and remembers
- Thanks to these study participants, we are getting unprecedented access to the human brain in action

Bradley Lega's group at the University of Texas Southwestern Medical Center identified "time cells" that are critical for remembering experiences, or episodic memory



Umbach et al, PNAS, 2020

NINDS researchers led by Kareem Zaghloul discovered that cell firing patterns that occur during learning are replayed shortly before remembering



Vaz et al, Science, 2020

Seizures associated with COVID-19

Annals of NEUROLOGY

An Official Journal of the American Neurological Association and the Child Neurology Society

ANA AMERICAN NEUROLOGICAL ASSOCIATION

Research Article | Free Access

Electroencephalographic Abnormalities are Common in COVID-19 and are Associated with Outcomes

Lu Lin MD, PhD, Abrar Al-Faraj MD, Neishay Ayub MD, Pablo Bravo MD, Sudeshna Das PhD, Lorenzo Ferlini MD, Ioannis Karakis MD, PhD, Jong Woo Lee MD, PhD, Shibani S. Mukerji MD, PhD, Christopher R. Newey DO, MS, Jay Pathmanathan MD, Myriam Abdennadher MD, Charles Casassa MD, Nicolas Gaspard MD, PhD, Daniel M. Goldenholz MD, PhD, Emily J. Gilmore MD, Jin Jing PhD, Jennifer A. Kim MD, PhD, Eyal Y. Kimchi MD, PhD, Harshad S. Ladha MD, Steven Tobochnik MD, Sahar Zafar MD, Lawrence J. Hirsch MD, M. Brandon Westover MD, PhD, Mouhsin M. Shafi MD, PhD ... See fewer authors

-Retrospective study of 197 patients with COVID-19 undergoing clinically indicated continuous electroencephalogram (cEEG) monitoring at 9 participating centers.

-Seizures were not uncommon in patients with COVID-19 undergoing cEEG, particularly in patients with a prior history of neurologic disease or significant abnormalities on neuroimaging.

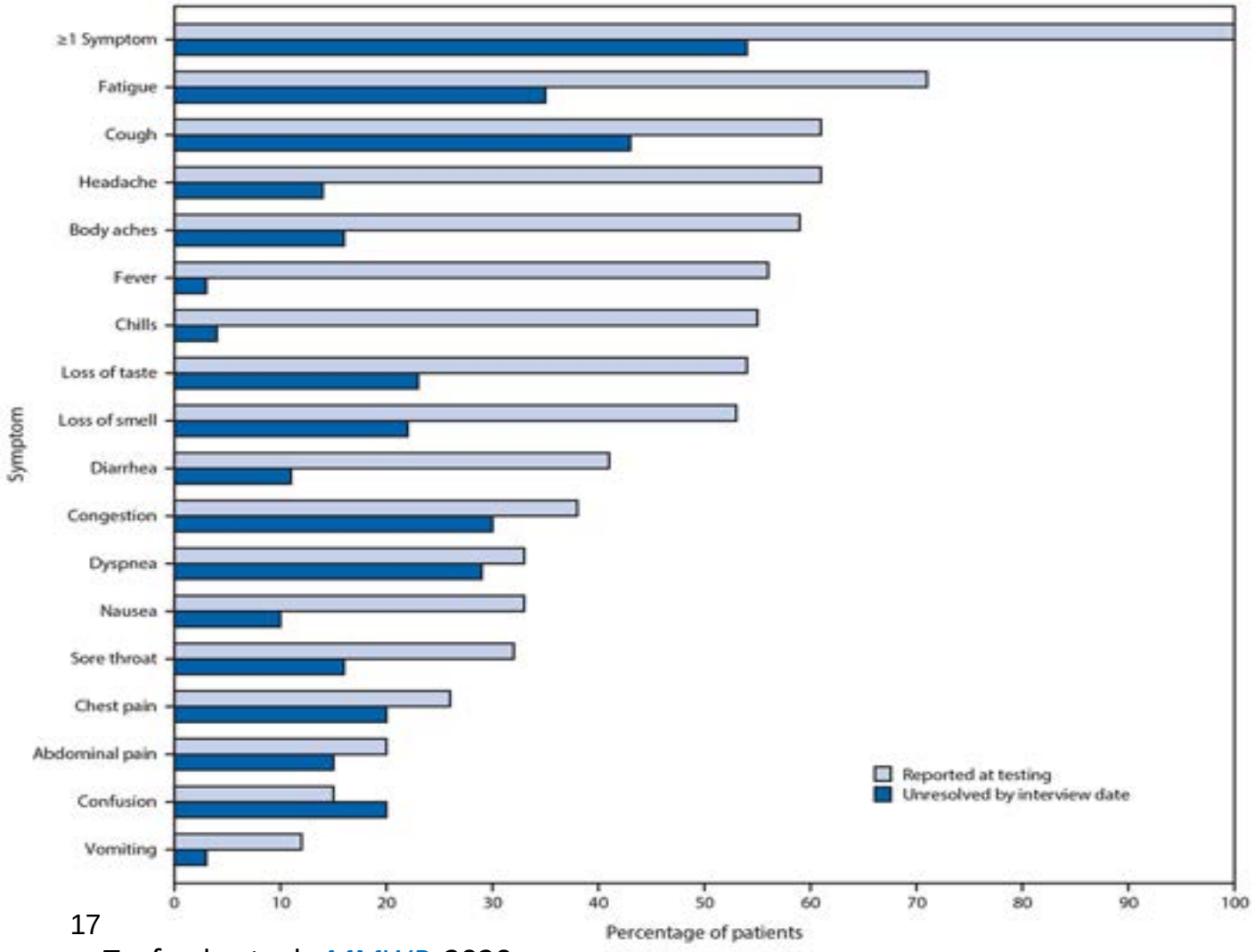
-Epileptiform abnormalities were common, occurring in almost 50% of monitored patients

-Seizures were associated with increased mortality, and NCSE was associated with prolonged length of stay

Annals of Neurology, Volume: 89, Issue: 5, Pages: 872-883,
First published: 11 March 2021, DOI: (10.1002/ana.26060)

NIH

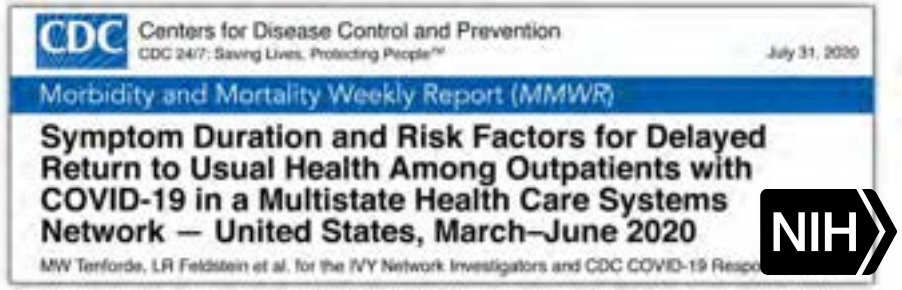
Persistent Symptoms of COVID-19 in Non-hospitalized Patients



Tenforde et. al., *MMWR*, 2020

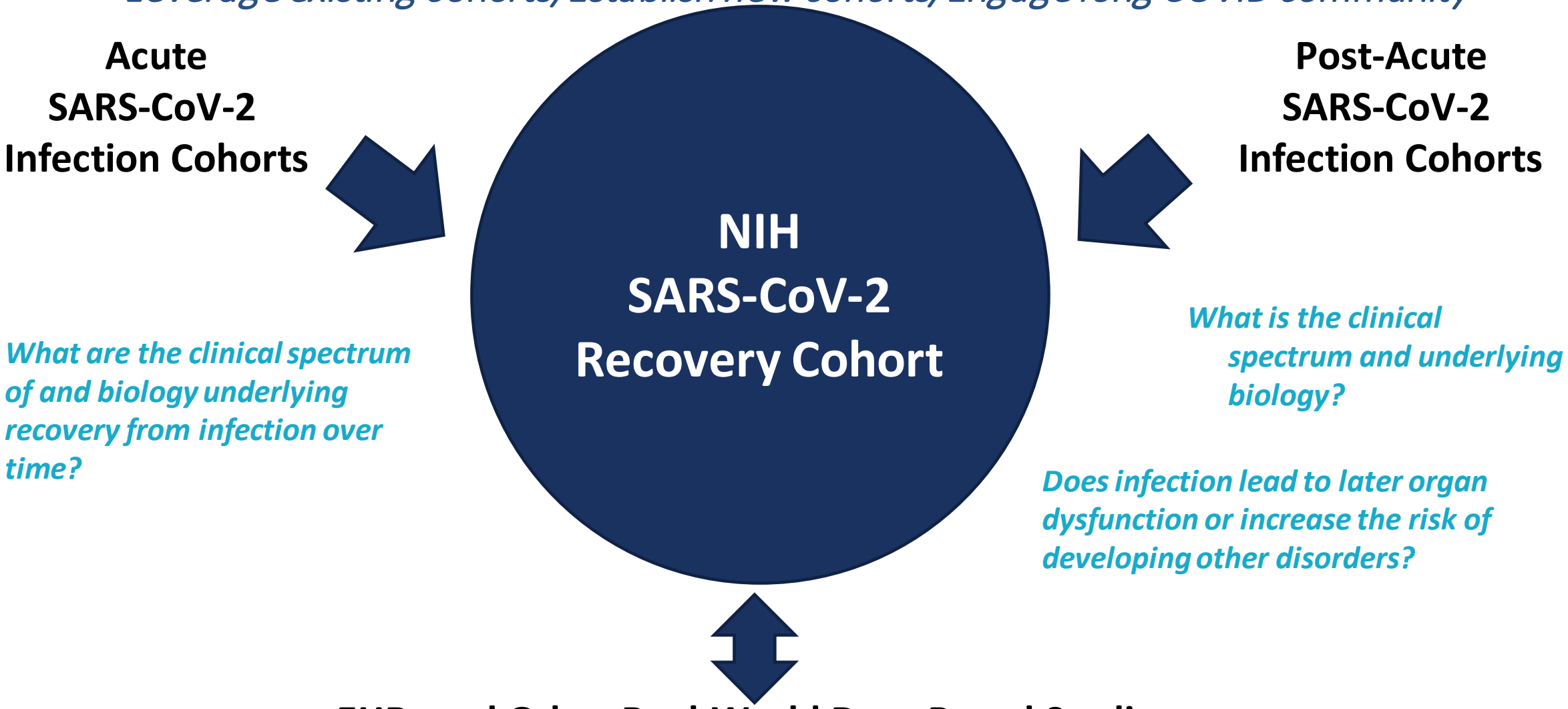
Symptomatic non-hospitalized patients with positive test for SARS-CoV-2:

- 35% not returned to baseline health 2-3 weeks after testing
- Older age and comorbidities associated with lack of return to baseline health
- 19% of young adults (18-34) with no comorbidities had not returned to baseline health
- In contrast 90% of influenza outpatients recover within 2 weeks



PASC Recovery Cohorts— "Meta-cohort"

Leverage existing cohorts/Establish new cohorts/Engage long COVID community



Thank you!

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